ELECTRONIC SUPPLEMENTARY MATERIAL

Neves Briard J *et al.*: Diagnostic accuracy of ancillary tests for death by neurologic criteria: a systematic review and meta-analysis

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eAppendix 1 Study search strategy

Database: Ovid MEDLINE(R) ALL 1946 to February 4, 2022
Date search conducted: February 5, 2022
Strategy:
1 Brain Death/ (9100)
2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).kw,sh,tw. (2216)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).kw,sh,tw. (21586)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).kw,sh,tw. (306)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).kw,sh,tw. (2)
6 comatose patient*.kw,sh,tw. (1884)
7 or/1-6 (27463)
8 exp "Sensitivity and Specificity"/ (629809)
9 (sensitiv* or specificity or accurac*).kw,sh,tw. (2270870)
10 (predictive adj3 value*).kw,sh,tw. (124929)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).kw,sh,tw. (92044)
12 (observer adj variation*).kw,sh,tw. (1321)
13 (roc adj curve*).kw,sh,tw. (44016)
14 (likelihood adj3 ratio*).kw,sh,tw. (17989)
15 likelihood function/ (23138)
16 diagnosis, differential/ or exp Diagnostic errors/ (573368)
17 (diagnostic error* or misdiagnos*).kw,sh,tw. (73366)
18 or/8-17 (3076024)
19 four-vessel angiograph*.kw,sh,tw. (136)
20 Technetium Tc-99m Exametazime/ (2977)
21 Tomography, Emission-Computed, Single-Photon/ (31958)
22 (single photon emission computed tomography or single photon emission ct or spect).kw,sh,tw. (35350)
23 Angiography, Digital Subtraction/ (11196)
24 digital subtraction angiograph*.kw,sh,tw. (9316)
25 Positron-Emission Tomography/ (58517)
26 Radionuclide Angiography/ (1188)
27 (Xenon computed tomography or xenon ct).kw,sh,tw. (360)
28 Magnetic Resonance Angiography/ (24156)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).kw,sh,tw. (28413)
30 (computed tomography angiography or ct angiography).kw,sh,tw. (29959)
31 (computed tomography perfusion or ct perfusion).kw,sh,tw. (2697)
32 Ultrasonography, Doppler, Transcranial/ (7843)
33 Transcranial Doppler.kw,sh,tw. (8772)
34 ancillary test$.kw,sh,tw. (1749)
35 ((brain or cerebral) adj perfusion).kw,sh,tw. (14458)
36 Electroencephalography/ (154498)
37 (Electroencephalography or eeg).kw,sh,tw. (182040)
38 exp Evoked Potentials/ (121786)
39 (evoked potentials or evoked response).kw,sh,tw. (82262)
40 or/19-39 (462185)
41 7 and 18 (3687)
42 7 and 40 (3377)
43 41 or 42 [Ancillary testing for diagnosis of brain death SR search] (6157)
44 (case reports not review).pt. (2108675)
45 43 not 44 [Exclude case reports] (5318)

Database: Ovid Embase Classic+Embase 1947 to 2022 February 03
Date search conducted: February 5, 2022

Strategy:
1 brain death/ (16023)
2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).kw,sh,tw. (3368)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).kw,sh,tw. (68821)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).ti,ab. (432)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).kw,sh,tw. (1)
6 comatose patient*.kw,sh,tw. (4705)
7 or/1-6 (79058)
8 "sensitivity and specificity"/ (420601)
9 (sensitiv* or specificity or accurac*).ti,ab. (2709512)
10 (predictive adj3 value*).kw,sh,tw. (187405)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).kw,sh,tw. (175127)
12 (observer adj variation*).kw,sh,tw. (2053)
13 (roc adj curve*).kw,sh,tw. (75929)
14 (likelihood adj3 ratio*).kw,sh,tw. (24484)
15 differential diagnosis/ (411284)
16 Diagnostic errors/ (62447)
17 (diagnostic error* or misdiagnos*).kw,sh,tw. (101875)
18 or/8-17 (3493601)
19 four-vessel angiograph*.kw,sh,tw. (170)
20 hexamethylpropylene amine oxime technetium Tc-99m/ (5146)
21 single photon emission computed tomography/ (13691)
22 (single photon emission computed tomography or single photon emission ct or spect).kw,sh,tw. (62187)
23 digital subtraction angiography/ (24901)
24 digital subtraction angiograph*.kw,sh,tw. (26979)
25 positron emission tomography/ (149893)
26 radionuclide ventriculography/ (651)
27 (Xenon computed tomography or xenon ct).kw,sh,tw. (459)
28 magnetic resonance angiography/ (39056)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).kw,sh,tw. (42373)
30 (computed tomography angiography or ct angiography).kw,sh,tw. (35078)
31 (computed tomography perfusion or ct perfusion).kw,sh,tw. (4875)
32 transcranial Doppler ultrasonography/ (2610)
33 Transcranial Doppler.kw,sh,tw. (14470)
34 ancillary test$.kw,sh,tw. (2769)
35 ((brain or cerebral) adj perfusion).kw,sh,tw. (21704)
36 electroencephalography/ (133171)
37 (Electroencephalography or eeg).kw,sh,tw. (224037)
38 exp Evoked Potentials/ (81078)
39 (evoked potentials or evoked response).kw,sh,tw. (81561)
40 or/19-39 (635766)
41 7 and 18 (12583)
42 7 and 40 (8210)
43 41 or 42 (18891)
44 case report/ (2804713)
45 43 not 44 [Exclude case reports] (16149)
46 limit 45 to embase (7461)

Database: EBM Reviews - ACP Journal Club 1991 to November 2021, EBM Reviews - Cochrane Central Register of Controlled Trials November 2021, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to December 02, 2021
Date search conducted: February 5, 2022
Strategy:
1 Brain Death/ (88)

2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).af. (159)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).af. (1889)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).ti,ab. (7)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).af. (0)
6 comatose patient*.af. (294)
7 or/1-6 (2223)
8 exp "Sensitivity and Specificity"/ (16963)
9 (sensitiv* or specificity or accurac*).ti,ab. (98252)
10 (predictive adj3 value*).af. (18329)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).af. (6885)
12 (observer adj variation*).af. (2578)
13 (roc adj curve*).af. (3650)
14 (likelihood adj3 ratio*).af. (1555)
15 likelihood function/ (340)
16 diagnosis, differential/ or exp Diagnostic errors/ (4410)
17 (diagnostic error* or misdiagnos*).af. (1462)
18 or/8-17 (122960)
19 four-vessel angiograph*.af. (3)
20 Technetium Tc-99m Exametazime/ (101)
21 Tomography, Emission-Computed, Single-Photon/ (1033)
22 (single photon emission computed tomography or single photon emission ct or spect).af. (2622)
23 Angiography, Digital Subtraction/ (230)
24 digital subtraction angiograph*.af. (598)
25 Positron-Emission Tomography/ (1034)
26 Radionuclide Angiography/ (64)
27 (Xenon computed tomography or xenon ct).af. (28)
28 Magnetic Resonance Angiography/ (455)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).af. (1080)
30 (computed tomography angiography or ct angiography).af. (1965)
31 (computed tomography perfusion or ct perfusion).af. (357)
32 Ultrasonography, Doppler, Transcranial/ (459)
33 Transcranial Doppler.af. (1382)
34 ancillary test$.af. (58)
35 ((brain or cerebral) adj perfusion).af. (1469)
36 Electroencephalography/ (4863)
37 (Electroencephalography or eeg).af. (11973)
38 exp Evoked Potentials/ (3303)
39 (evoked potentials or evoked response).af. (5013)
40 or/19-39 (25429)
41 7 and 18 (256)
42 7 and 40 (255)
43 41 or 42 (445)

Database: CINAHL Ebsco (1981 to February 4, 2022)
Date search conducted: February 5, 2022
Strategy:

#	Query	Limiters/Expanders	Results
S1	(MH "Brain Death") OR ((cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*)) OR (((brain* or neurol*) N3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*))) OR (((coma* or stupor) N2	Search modes - Boolean/Phrase	7,590

	(irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).) OR (((unarous* or un-arous*) N2 (unrespons* or un-respons*))) OR comatose patient*		
S2	((MH "Sensitivity and Specificity") OR (MH "Diagnosis, Differential") OR (MH "Diagnostic Errors")) OR ((sensitiv* or specificity or accurac*)) OR (predictive N3 value*) OR (((true N positive*) or (false N positive*) or (false N negative*) or (true N negative*) or diagnos* determination of death or ((diagnos* or determination) N2 death))) OR (observer adj variation*) OR (roc adj curve*) OR (likelihood adj3 ratio*) OR ((diagnostic error* or misdiagnos*))	Search modes - Boolean/Phrase	457,289
S3	(MH "Angiography, Digital Subtraction") OR (MH "Tomography, Emission-Computed") OR (MH "Radionuclide Ventriculography") OR (MH "Magnetic Resonance Angiography") OR (MH "Ultrasonography, Doppler, Transcranial") OR (MH "Electroencephalography") OR (MH "Evoked Potentials") OR (MH "Evoked Potentials, Auditory, Brainstem") OR (MH "Evoked Potentials, Motor") OR (MH "Evoked Potentials, Visual") OR (MH "Evoked Potentials, Somatosensory") OR (MH "Evoked Potentials, Auditory") OR (MH "Auditory Steady-State Response")	Search modes - Boolean/Phrase	56,760
S4	S1 AND S2	Search modes - Boolean/Phrase	1,724
S5	S1 AND S3	Search modes - Boolean/Phrase	578
S6	S4 OR S5	Search modes - Boolean/Phrase	2,046
S7	(MH "Case Studies")	Search modes - Boolean/Phrase	25,470
S8	TI((case N1 (report or study) NOT review)	Search modes - Boolean/Phrase	87,009
S9	S7 OR S8	Search modes - Boolean/Phrase	108,409
S10	S6 NOT S9	Search modes - Boolean/Phrase	2,014

eAppendix 2 Model details and Stan code

Below we present the technical details pertaining to the models and Stan code used in the meta-analysis.

Meta-analysis of clinically diagnosed death by neurologic criteria patients

Following Kruschke and Vanpaemel, we specify our hierarchical model as follows [1]. We index test types with *i* and assessments with *j*. Thus, μ_i represents the sensitivity for test type *i*, while θ_{ij} represents the sensitivity for assessment *j* of test type *i*. Of course, μ represents the overall sensitivity across all test types.

Our observations consist of x_{ij}, the number of true positives for assessment *j* of test type *i* and m_{ij}, the sum of the number of true positives and false negatives for assessment *j* of test type *i*.

Here is the model specification:

Likelihood / observation model

$$x_{ij} \sim \text{Binomial}(m_{ij}, \theta_{ij}).$$

Hierarchical priors

$$\theta_{ij} \sim \text{Beta}(\alpha_i, \beta_i), \text{ where}$$

$$\alpha_i = \mu_i\kappa_\mu \text{ and } \beta_i = (1 - \mu_i)\kappa_\mu.$$

Following Kruschke and Vanpaemel, we will parametrize in terms of μ_i and κ_μ.

$$\mu_i \sim \text{Beta}(\alpha, \beta), \text{ where}$$

$$\alpha = \mu\kappa \text{ and } \beta = (1 - \mu)\kappa.$$

Top-level priors

$$\mu \sim \text{Beta}(1, 1),$$

$$\kappa_\mu \sim \text{half Cauchy}(150), \text{and}$$

$$\kappa \sim \text{half Cauchy}(150).$$

Finally, we can compute the variances as follows:

$$\sigma_i^2 = \frac{\alpha_i\beta_i}{(\alpha_i+\beta_i)^2(\alpha_i+\beta_i+1)}, \text{ and}$$

$$\sigma^2 = \frac{\alpha\beta}{(\alpha+\beta)^2(\alpha+\beta+1)}.$$

Meta-analysis of clinically suspected death by neurologic criteria patients

Following Rutter and Gatsonis (adapted to the three-level case), we specify our hierarchical model as follows [2]. We index test types with *i*, assessments with *j*, and the true disease status with *k* (1: Comatose, 2: Death by neurologic criteria). Thus, π_{ij2} represents the sensitivity for assessment *j* of test type *i*, and $1 - \pi_{ij1}$ represents the specificity for assessment *j* of test type *i*.

Our observations consist of y_{ijk}, the number of cases from population *k* classified as positive for assessment *j* of test type *i*, n_{ijk}, the total number of cases from population *k* for assessment *j* of test type *i*, and x_{ijk}, the indicator of death by neurologic criteria for population *k* for assessment *j* of test type *i*.

Here is the model specification:

Likelihood / observation model

$$y_{ijk} \sim \text{Binomial}(n_{ijk}, \pi_{ijk}), \text{ where}$$

$$\text{logit}(\pi_{ijk}) = \frac{\theta_{ij}+\alpha_{ij}x_{ijk}}{e^{\beta x_{ijk}}}, \text{ and}$$

$$x_{ij1} = -0.5 \text{ and } x_{ij2} = 0.5.$$

Hierarchical priors

$$\theta_{ij} \sim \text{Normal}(\theta_i, \sigma_\theta),$$

$$\theta_i \sim \text{Normal}(\theta, \tau_\theta),$$

$$\alpha_{ij} \sim \text{Normal}(\alpha_i, \sigma_\alpha), \text{ and}$$

$$\alpha_i \sim \text{Normal}(\alpha, \tau_\alpha).$$

Top-level priors

$$\theta \sim \text{Normal}(0, 10),$$

$$\alpha \sim \text{Normal}(2.5, 5),$$

$$\beta \sim Normal(0, 5), \text{ and}$$

$$\sigma_\theta, \sigma_\alpha, \tau_\theta, \tau_\theta \sim \text{Gamma}(1.00625, 0.0625).$$

A short discussion of these top-level priors is in order. The parameters α, β, and θ respectively represent the diagnostic accuracy, asymmetry, and the positivity threshold for the ROC curve. The parameters σ_α and τ_α respectively represent the between-study and between-test standard deviations of the diagnostic accuracy parameter. Similarly, the parameters σ_θ and τ_θ respectively represent the between-study and between-test standard deviations of the positivity threshold parameter.

The range of sensible (i.e., non-extreme) values is about 0 to 5 for diagnostic accuracy and -1 to 1 for asymmetry. For the positivity threshold, a range of -10 to 10 is generally sufficient to plot the entire ROC curve across the possible range of sensitivity and specificity. This suggests a starting point for priors would be to pick a mean at the center of those ranges and set the standard deviations such that the endpoints of the ranges are one or two standard deviations from the mean. The priors we chose for our analysis are substantially loosened versions of these.

For the standard deviation parameters, we chose to use Gamma priors instead of half-Cauchy ones in order to set the mode of the prior away from zero to protect against potential implosive shrinkage of the random effects toward their respective means. This precaution was deemed particularly necessary for this model, since the ratio of data quantity to model complexity was considered relatively low. The Gamma priors were initially chosen to be relatively similar to half-Cauchy ones based on the sensible parameter ranges discussed above. The priors used for our analyses were then loosened considerably from those versions.

Fixed effect estimates for Rutter-Gatsonis model

Parameter	Posterior mode and 95% HDI
$\boldsymbol{\theta}$	-0.21 (-1.67 to 1.39)
$\boldsymbol{\alpha}$	8.24 (6.65 to 10.51)
$\boldsymbol{\beta}$	0.71 (0.13 to 1.43)
$\boldsymbol{\sigma_\alpha}$	2.55 (1.56 to 3.94)
$\boldsymbol{\tau_\alpha}$	0.13 (0.00 to 2.04)
$\boldsymbol{\sigma_\theta}$	1.19 (0.63 to 2.01)
$\boldsymbol{\tau_\theta}$	2.20 (1.21 to 3.89)

Stan code for meta-analysis of clinically diagnosed death by neurologic criteria patients

```
data {
    int<lower=0> N;         // Total number of assessments
    int<lower=0> I;         // Total number of test types
    int<lower=0> x[N];      // Numerator (TP)
    int<lower=0> m[N];      // Denominator (TP + FN)
    int<lower=0> test[N];   // Index for test types
    real<lower=0> scale_prior; // Half-Cauchy prior's scale (150)
}
parameters {
    // Pooled sensitivity estimates (no trade-off with specificity)
    real<lower=0,upper=1> theta[N];    // Assessment level
    vector<lower=0,upper=1>[I] mu_i;   // Test type level
    real<lower=0,upper=1> mu;          // Overall
    // Re-parameterized Beta scale/concentration parameters
    real<lower=0> kappa_mu;  // Within-test concentration
    real<lower=0> kappa;     // Between-test concentration
}
transformed parameters {
    vector<lower=0>[I] alpha_i;
    vector<lower=0>[I] beta_i;
    vector<lower=0>[I] sigma_i;
    real<lower=0> alpha;
    real<lower=0> beta;
    real<lower=0> sigma;
    // Transforming back from re-parametrization
    alpha_i = mu_i * kappa_mu;
    beta_i = (1 - mu_i) * kappa_mu;
    alpha = mu * kappa;
    beta = (1 - mu) * kappa;
    // Convert to standard deviations
    for (i in 1:I) {
      sigma_i[i] = sqrt(
        (alpha_i[i] * beta_i[i]) /
        (square(alpha_i[i] + beta_i[i]) * (alpha_i[i] + beta_i[i] + 1))
                  );
    }
    sigma = sqrt((alpha * beta) /
                 (square(alpha + beta) * (alpha + beta + 1)));
}
model {
    // Top-level priors
    // Overall sensitivity
    target += beta_lpdf(mu | 1 , 1); // ~ unif(0, 1)
    // Between assessment/test type concentration
    // half-Cauchy (i.e., folded at location zero)
    target += cauchy_lpdf(kappa_mu | 0 , scale_prior);
    target += cauchy_lpdf(kappa | 0 , scale_prior);

    // Hierarchical priors
    // Test types nested within overall
    for (i in 1:I) {
      target += beta_lpdf(mu_i[i] | alpha , beta);
```

```
    }

    // Assessments nested within test types
    for (n in 1:N) {
      target += beta_lpdf(theta[n] | alpha_i[test[n]] , beta_i[test[n]]);
    }

    // Likelihood / observation model
    target += binomial_lpmf(x | m , theta);
}
generated quantities {
    // posterior predictive check
    int<lower=0> xhat[N]; // TP's given TP+FN and sensitivity
    real<lower=0,upper=1> yhat[N];
    for (n in 1:N) {
      xhat[n] = binomial_rng(m[n], theta[n]);
      yhat[n] = (xhat[n] + 0.0) / m[n];
    }
}
```

Stan code for meta-analysis of clinically suspected death by neurologic criteria patients

```
data {
    int<lower=0> N;       // Total number of assessments
    int<lower=0> I;       // Total number of test types
    int<lower=0> test[N]; // Index for test types
    int<lower=0> y_ij1[N]; // Number classified as positive among non-
diseased
    int<lower=0> y_ij2[N]; // Number classified as positive among diseased
    int<lower=0> n_ij1[N]; // Number non-diseased
    int<lower=0> n_ij2[N]; // Number diseased
    vector[2] x; // Indicator of true disease status (-0.5 for non-
diseased, 0.5 for diseased)
    // Prior parameters
    real alpha_prior_mu;
    real<lower=0> alpha_prior_sigma;
    real beta_prior_mu;
    real<lower=0> beta_prior_sigma;
    real theta_prior_mu;
    real<lower=0> theta_prior_sigma;
    real<lower=0> sd_alpha_shape;
    real<lower=0> sd_alpha_rate;
    real<lower=0> sd_theta_shape;
    real<lower=0> sd_theta_rate;
}
parameters {
    // Assessment level
    real alpha_ij_raw[N];
    real theta_ij_raw[N];
    // Test type level
    real alpha_i_raw[I];
    real theta_i_raw[I];
    // Overall
    real alpha;
    real theta;
    real beta;
    // Scale parameters
    // Within-test heterogeneity
    real<lower=0> sigma_alpha;
    real<lower=0> sigma_theta;
    // Between-test heterogeneity
    real<lower=0> tau_alpha;
    real<lower=0> tau_theta;
}
transformed parameters {
    // Overall sensi and speci
    real<lower=0,upper=1> p_1;
    real<lower=0,upper=1> p_2;
    // Ancillary test level sensi and speci
    real<lower=0,upper=1> p_i1[I];
    real<lower=0,upper=1> p_i2[I];
    // Linear predictor
    real<lower=0,upper=1> p_ij1[N];
    real<lower=0,upper=1> p_ij2[N];
```

```
    // Re-centering hierarchical parameters
    real alpha_ij[N];
    real theta_ij[N];
    real alpha_i[I];
    real theta_i[I];
    for (i in 1:I) {
        alpha_i[i] = alpha + (tau_alpha * alpha_i_raw[i]);
        theta_i[i] = theta + (tau_theta * theta_i_raw[i]);
        p_i1[i] = inv_logit((theta_i[i] + (alpha_i[i] * x[1])) / exp(beta
* x[1]));
        p_i2[i] = inv_logit((theta_i[i] + (alpha_i[i] * x[2])) / exp(beta
* x[2]));
    }
    for (n in 1:N) {
        alpha_ij[n] = alpha_i[test[n]] + (sigma_alpha * alpha_ij_raw[n]);
        theta_ij[n] = theta_i[test[n]] + (sigma_theta * theta_ij_raw[n]);
        p_ij1[n] = inv_logit((theta_ij[n] + (alpha_ij[n] * x[1])) /
exp(beta * x[1]));
        p_ij2[n] = inv_logit((theta_ij[n] + (alpha_ij[n] * x[2])) /
exp(beta * x[2]));
    }
    p_1 = inv_logit((theta + (alpha * x[1])) / exp(beta * x[1]));
    p_2 = inv_logit((theta + (alpha * x[2])) / exp(beta * x[2]));
}
model {
    // Top-level priors
    target += gamma_lpdf(sigma_alpha | sd_alpha_shape, sd_alpha_rate);
    target += gamma_lpdf(sigma_theta | sd_theta_shape, sd_theta_rate);
    target += gamma_lpdf(tau_alpha | sd_alpha_shape, sd_alpha_rate);
    target += gamma_lpdf(tau_theta | sd_theta_shape, sd_theta_rate);
    target += normal_lpdf(alpha | alpha_prior_mu, alpha_prior_sigma);
    target += normal_lpdf(theta | theta_prior_mu, theta_prior_sigma);
    target += normal_lpdf(beta | beta_prior_mu, beta_prior_sigma);

    // Hierarchical priors
    target += normal_lpdf(alpha_i_raw | 0, 1);  // alpha_i ~ normal(alpha,
tau_alpha)
    target += normal_lpdf(theta_i_raw | 0, 1);  // theta_i ~ normal(theta,
tau_theta)
    target += normal_lpdf(alpha_ij_raw | 0, 1); // alpha_ij ~
normal(alpha_i, sigma_alpha)
    target += normal_lpdf(theta_ij_raw | 0, 1); // theta_ij ~
normal(theta_i, sigma_theta)

    // Likelihood / observation model
    target += binomial_lpmf(y_ij1 | n_ij1, p_ij1);
    target += binomial_lpmf(y_ij2 | n_ij2, p_ij2);
}
generated quantities {
    // posterior predictive check
    real<lower=0,upper=1> r_ij1_hat[N];
    real<lower=0,upper=1> r_ij2_hat[N];
    // Test statistics
    real r_ij1_hat_mean;
```

```
    real r_ij1_hat_sd;
    real r_ij1_hat_min;
    real r_ij1_hat_max;
    real r_ij2_hat_mean;
    real r_ij2_hat_sd;
    real r_ij2_hat_min;
    real r_ij2_hat_max;
    for (n in 1:N) {
        r_ij1_hat[n] = (binomial_rng(n_ij1[n], p_ij1[n]) + 0.0) /
n_ij1[n];
        r_ij2_hat[n] = (binomial_rng(n_ij2[n], p_ij2[n]) + 0.0) /
n_ij2[n];
    }
    r_ij1_hat_mean = mean(r_ij1_hat);
    r_ij1_hat_sd = sd(r_ij1_hat);
    r_ij1_hat_min = min(r_ij1_hat);
    r_ij1_hat_max = max(r_ij1_hat);
    r_ij2_hat_mean = mean(r_ij2_hat);
    r_ij2_hat_sd = sd(r_ij2_hat);
    r_ij2_hat_min = min(r_ij2_hat);
    r_ij2_hat_max = max(r_ij2_hat);
}
```

eAppendix 3 Justification for study exclusions

Study and reference	Reason for exclusion
Abdel-Dayem 1989 [3]	No *a priori* definition of the ancillary test diagnostic criteria
Akdogan 2020 [4]	No *a priori* definition of the ancillary test diagnostic criteria
Altinsoy 2020 [5]	Not a diagnostic accuracy study
An 2019 [6]	Not a diagnostic accuracy study
Andic 2020 [7]	Not a diagnostic accuracy study
Archila-Rincon 2018 [8]	Not an ancillary test of interest
Attamimi 2021 [9]	Not a diagnostic accuracy study
Baidya 2018 [10]	Insufficient information on reference standard
Berlit 1990 [11]	Data included in Berlit 1992
Berthier 2017 [12]	Not a diagnostic accuracy study
Blanot 2016 [13]	Not the study population of interest
Bohatyrewicz 2010 [14]	Data included in Sawicki 2015a, Sawicki 2018 and Sawicki 2019 (confirmed with authors)
Bohatyrewicz 2013 [15]	Data included in Sawicki 2015a and Sawicki 2018 (confirmed with authors)
Bohatyrewicz 2017 [16]	Data included in Sawicki 2015a and Sawicki 2018 (confirmed with authors)
Bohatyrewicz 2019 [17]	Data included in Sawicki 2015a, Sawicki 2018 and Sawicki 2019 (confirmed with authors)
Bohatyrewicz 2021 [18]	Not a diagnostic accuracy study
Brasil 2016 [19]	Not a diagnostic accuracy study
Brasil 2018 [20]	Not a diagnostic accuracy study
Braunstein 1973 [21]	Insufficient information on reference standard
Brunser 2010 [22]	Data included in Brunser 2015
Buchner 1988 [23]	No *a priori* definition of the ancillary test diagnostic criteria
Buchner 2016 [24]	Not a diagnostic accuracy study
Cabrera Suarez 2018 [25]	Not a diagnostic accuracy study
Cacciatori 2018a [26]	Not a diagnostic accuracy study
Cacciatori 2018b [27]	Insufficient information on reference standard
Cacciatori 2020 [28]	Insufficient information on reference standard
Caccioppola 2018 [29]	No *a priori* definition of the ancillary test diagnostic criteria
Carella 1973 [30]	Not an ancillary test of interest
Casadio 2017a [31]	No *a priori* definition of the ancillary test diagnostic criteria
Casadio 2017b [32]	Abstract of a published full-text manuscript
Cestari 2018 [33]	Not a diagnostic accuracy study
Chang 2016 [34]	Not a diagnostic accuracy study
Chawla 2017 [35]	Not a diagnostic accuracy study
Cramaro 2015 [36]	Insufficient information on reference standard
Cuesta 2017 [37]	Insufficient information on reference standard
de Freitas 2003 [38]	Data included in de Freitas 2006
de la Riva 1992 [39]	Insufficient information on reference standard
de Tribolet 1977 [40]	Not an ancillary test of interest
Dominguez-Roldan 1995 [41]	No *a priori* definition of the ancillary test diagnostic criteria
Dominguez-Roldan 2004 [42]	Data included in Dominguez-Roldan 1995
Ducrocq 1989 [43]	Data included in Ducrocq 1998
Ducrocq 1992 [44]	Data included in Ducrocq 1998
Duric 2013 [45]	No *a priori* definition of the ancillary test diagnostic criteria
Elmas 1995 [46]	Insufficient information on reference standard
Elmer 2020 [47]	Not a diagnostic accuracy study
Erbengi 1990 [48]	Data included in Erbengi 1991
Erbengi 1991 [49]	No *a priori* definition of the ancillary test diagnostic criteria
Escudero 2007 [50]	Data included in Escudero 2009

Escudero 2015 [51]	Not a diagnostic accuracy study
Facco 1988 [52]	Data included in Facco 2002
Facco 1990 [53]	Data included in Facco 2002
Facco 2002 [54]	No *a priori* definition of the ancillary test diagnostic criteria
Feldges 1990 [55]	Insufficient information on reference standard
Fernandes 2017 [56]	Insufficient information on reference standard
Firsching 1987 [57]	Data included in Firsching 1992
Firsching 1992a [58]	No *a priori* definition of the ancillary test diagnostic criteria
Firsching 1992b [59]	No *a priori* definition of the ancillary test diagnostic criteria
Flowers 2000 [60]	Data included in Flowers 1997
Fotiou 1987 [61]	No *a priori* definition of the ancillary test diagnostic criteria
Francis 2010 [62]	Data not extractable
Garcia-Larrea 1987 [63]	No *a priori* definition of the ancillary test diagnostic criteria
Gobert 2018 [64]	Not a diagnostic accuracy study
Godoy Bravo 2017 [65]	Insufficient information on reference standard
Jorgensen 1974 [66]	Not the study population of interest
Hashemian 2014 [67]	Abstract of a published full-text manuscript
Herman 2020 [68]	Not a diagnostic accuracy study
Hoffmann 2016 [69]	No *a priori* definition of the ancillary test diagnostic criteria
Ishiyama 2019 [70]	Insufficient information on reference standard
Ishii 1996 [71]	No *a priori* definition of the ancillary test diagnostic criteria
Jouffroy 2017 [72]	No *a priori* definition of the ancillary test diagnostic criteria
Karacam 2017 [73]	Not a diagnostic accuracy study
Karasu 2015 [74]	Not a diagnostic accuracy study
Kaste 1979 [75]	Not a diagnostic accuracy study
Kavi 2016 [76]	Not the study population of interest
Kim 2015 [77]	Not a diagnostic accuracy study
Kojder 1998 [78]	No *a priori* definition of the ancillary test diagnostic criteria
Korein 1977 [79]	No *a priori* definition of the ancillary test diagnostic criteria
Kramer 2021 [80]	Insufficient information on reference standard
Kreitler 2015 [81]	Not a diagnostic accuracy study
Lechner 1997 [82]	No *a priori* definition of the ancillary test diagnostic criteria
Leclerc 2006 [83]	No *a priori* definition of the ancillary test diagnostic criteria
Lee 1987 [84]	Not an ancillary test of interest
Link 1988 [85]	Data included in Link 1988
Litscher 1995 [86]	No *a priori* definition of the ancillary test diagnostic criteria
Llompart-Pou 2009 [87]	No *a priori* definition of the ancillary test diagnostic criteria
Luchtmann 2013 [88]	No *a priori* definition of the ancillary test diagnostic criteria
Luchtmann 2014 [89]	No *a priori* definition of the ancillary test diagnostic criteria
Machado 1991 [90]	No *a priori* definition of the ancillary test diagnostic criteria
Machado 1993a [91]	No *a priori* definition of the ancillary test diagnostic criteria
Machado 1993b [92]	No *a priori* definition of the ancillary test diagnostic criteria
Machado 1993c [93]	No *a priori* definition of the ancillary test diagnostic criteria
Marinoni 2017 [94]	Not a diagnostic accuracy study
Marinoni 2018a [95]	Not a diagnostic accuracy study
Marinoni 2018b [96]	Not a diagnostic accuracy study
Marinoni 2020 [97]	Not a diagnostic accuracy study
Mauguiere 1982 [98]	No *a priori* definition of the ancillary test diagnostic criteria
Mesraoua 1992 [99]	No *a priori* definition of the ancillary test diagnostic criteria
Migdady 2020 [100]	Not a diagnostic accuracy study
Migdady 2021b [101]	Not a diagnostic accuracy study
Migdady 2021c [102]	Not a diagnostic accuracy study
Morimoto 1995 [103]	Not a diagnostic accuracy study

Mussachio 2010 [104]	Insufficient information on reference standard (additional information requested, but no reply from author)
Niu 2020 [105]	Not a diagnostic accuracy study
Okii 2009 [106]	Not a diagnostic accuracy study
Ouaknine 1973 [107]	Not a diagnostic accuracy study
Ouaknine 1985 [108]	Not a diagnostic accuracy study
Ozpar 2021 [109]	Insufficient information on reference standard
Pan 2021 [110]	No *a priori* definition of the ancillary test diagnostic criteria
Pang 2017 [111]	Not a diagnostic accuracy study
Paro 2013 [112]	Not a diagnostic accuracy study
Pastuszka 2015 [113]	Data included in Sawicki 2015a (confirmed with authors)
Peckham 2018 [114]	No *a priori* definition of the ancillary test diagnostic criteria
Petrovic 1991 [115]	No *a priori* definition of the ancillary test diagnostic criteria
Ray 2021 [116]	Not a diagnostic accuracy study
Reid 1989 [117]	Insufficient information on reference standard
Reid 1990 [118]	Insufficient information on reference standard
Robles-Caballero 2020 [119]	Insufficient information on reference standard
Ronconi 2021 [120]	Not a diagnostic accuracy study
Roncucci 1999 [121]	No *a priori* definition of the ancillary test diagnostic criteria
Sadeghian 2017 [122]	Not a diagnostic accuracy study
Sahin 2019 [123]	Not an ancillary test of interest
Samardzic 2017 [124]	No *a priori* definition of the ancillary test diagnostic criteria
Sayan 2020 [125]	Not a diagnostic accuracy study
Sawicki 2013 [126]	Data included in Sawicki 2015a, Sawicki 2018 and Sawicki 2019 (confirmed with authors)
Sawicki 2014 [127]	Data included in Sawicki 2015a and Sawicki 2018 (confirmed with authors)
Sawicki 2015b [128]	Data included in Sawicki 2019 (confirmed with authors)
Sawicki 2017 [129]	Data included in Sawicki 2015a, Sawicki 2018 and Sawicki 2019 (confirmed with authors)
Scarpino 2016 [130]	Abstract of a published full-text manuscript
Scarpino 2017a [131]	Not the study population of interest
Scarpino 2017b [132]	Insufficient information on reference standard
Scarpino 2017c [133]	Abstract of a published full-text manuscript
Selcuk 2012 [134]	No *a priori* definition of the ancillary test diagnostic criteria
Schober 1987 [135]	No *a priori* definition of the ancillary test diagnostic criteria
Shan 1999 [136]	Not a diagnostic accuracy study
Shankar 2020 [137]	Not the study population of interest
Sharma 2010 [138]	Insufficient information on reference standard
Sirucek 2017 [139]	Insufficient information on reference standard
Solek-Pastuska 2021 [140]	Not a diagnostic accuracy study
Spieth 1994 [141]	Insufficient information on reference standard
Starr 1976 [142]	No *a priori* definition of the ancillary test diagnostic criteria
Su 2003 [143]	Data included in Su 2014
Taylor 2018 [144]	Not a diagnostic accuracy study
Toscano 2017 [145]	Insufficient information on reference standard
Trigo 2017 [146]	Data not extractable
Trojaborg 1973 [147]	No *a priori* definition of the ancillary test diagnostic criteria
Tsivgoulis 2015 [148]	Not a diagnostic accuracy study
Valdes 2020 [149]	Not a diagnostic accuracy study
Valentin 1997 [150]	Not the study population of interest
Varelas 2021 [151]	Not a diagnostic accuracy study
Venkatram 2015 [152]	Article retracted by journal/authors
Vincenzini 2013 [153]	Not the study population of interest
Wagner 1990 [154]	No *a priori* definition of the ancillary test diagnostic criteria

Wagner 1996 [155]	No *a priori* definition of the ancillary test diagnostic criteria
Wang 2012 [156]	Data included in Wang 2008
Welschehold 2012a [157]	Data included in Welschehold 2013b
Welschehold 2012b [158]	Data included in Welschehold 2013a and Welschehold 2013b
Welschehold 2013c [159]	Data included in Welschehold 2013b
Yatim 1991 [160]	No *a priori* definition of the ancillary test diagnostic criteria
Yildirim 2020 [161]	No *a priori* definition of the ancillary test diagnostic criteria
Zampakis 2021 [162]	Not a diagnostic accuracy study
Zeitlhofer 1989 [163]	Not a diagnostic accuracy study
Zincircioglu 2020 [164]	Not a diagnostic accuracy study
Zheng 2009 [165]	Not a diagnostic accuracy study
Zhu 2019 [166]	Not a diagnostic accuracy study
Ziegler 2012 [167]	Not a diagnostic accuracy study
Zurynski 1989 [168]	No *a priori* definition of the ancillary test diagnostic criteria
Zurynski 1991 [169]	No *a priori* definition of the ancillary test diagnostic criteria

eAppendix 4 Characteristics of included studies

Study and reference	Study design	Patient population	Brain injury causes					Reference standard	DNC clinical examination criteria (explicitly stated, in addition to irreversible coma)				Ancillary test	DNC ancillary test criteria	Confounders	Delay between reference and ancillary tests
			CA	TBI	ICH	IS	Other		CNA	CP	PS	AT				
Akdogan 2021 [170]	Retrospective cohort	N=86, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 4 point scale	Lack of opacification of the middle cerebral arteries-M4 and internal cerebral veins evaluated at the venous phase	N	M
													CT-perfusion (CTP)	All evaluation was done qualitatively by the visual assessment of perfusion in cerebral blood flow and cerebral blood volume maps, which were acquired by automatic calculation. A matched complete absence of perfusion in both maps was interpreted as cerebral circulatory arrest.		
Al-Shammri 2004 [171]	Prospective cohort	n=28, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion with SPECT	Absent flow on dynamic study; nonvisualization of sagittal sinus; no uptake of the radiotracer within the brain regions on both planar and SPECT images.	Y	M

Algin 2015 [172]	Prospective cohort	n=22, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	Transcranial Doppler (TCD)	Doppler parameters were obtained from the middle cerebral artery. Resistive index >= 1.	N	M
													Other	Resistive index >=1.		
Ayim 1979 [173]	Retrospective cohort	n=30, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	N	Y	Y	Clinical examination	Y	Y	Y	Y	Electroencephalography (EEG) – Cortical	Isoelectric EEG.	Y	≥ 24 hours
Azevedo 2000 [174]	Retrospective cohort	n=97, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	Existence of diastolic flow reversal or just early systolic forward flow detected in three arteries of different territories or in only two of them when in the third one there was no longer any flow. This pattern should be present in a second evaluation with at least a 30-minute interval.	Y	M
Banzo 2012 [175]	Retrospective cohort	n=302, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	Radionuclide imaging – HMPAO perfusion without SPECT	Absence of supra- and infratentorial uptake in the planar images: any intracranial parenchymatous uptake rules out the diagnosis of encephalic death.	Y	M
													Radionuclide imaging – Tc-99 HMPAO	Absence of cerebral blood flow in the dynamic study.		

													angiography			
Barelli 1990 [176]	Unclear cohort	n=18, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Evoked potentials – Brainstem Auditory	Typical brain auditory evoked potential brain death patterns according to previous reports.	N	< 24 hours
Beltramello 2014 [177]	Unclear cohort	n=15, Clinically diagnosed death by neurologic criteria, Adults and children	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – 4 point scale CT-angiography (CTA) – no intracranial flow	A standardized technique for CTA was used, considering both the arterial and venous phases of CTA and a relative interpretative protocol which takes into consideration first the "arterial" phase (presence or absence of intracranial arteries: the so-called "stop at the siphon") and, only when proximal arteries are still opacified or undetectable due to coils or metal artifacts, the "French criteria" i.e. absence of opacification of M4-middle cerebral arteries and internal cerebral veins.	Y	M
Berenguer 2010 [178]	Prospective cohort	n=25, Clinically diagnosed death by	N	Y	N	Y	N	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – no	Absence of blood flow.	Y	< 24 hours

		neurologic criteria, Adults only											intracranial flow			
													Radionuclide imaging – other	Absence of blood flow.		
Bergquist 1972 [179]	Unclear cohort	n=28, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	N	Y	Y	Four-vessel angiography	Arrest of cerebral circulation.	Y	M
Berlit 1992 [180]	Unclear cohort	n=27, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	N	N	Y	Clinical examination	NR	NR	NR	NR	Four-vessel angiography	Not explicitly reported, but reference provided.	Y	≥ 24 hours
													Radionuclide imaging – HMPAO perfusion without SPECT	With cessation of cerebral circulation, the cranial cavity is represented as empty (the "hollow skull").		
													Transcranial Doppler (TCD)	Not explicitly reported, but reference provided.		
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
													Evoked potentials – Brainstem Auditory	Not explicitly reported, but reference provided.		
Bhattarai 2002 [181]	Prospective cohort	n=33, Clinically suspected death by neurologic criteria,	Y	Y	Y	N	N	Clinical examination	Y	N	N	Y	Evoked potentials – Brainstem Auditory	No identifiable brainstem auditory evoked potential waves at all or presence of wave-I only.	N	M

		Adults and children														
Bogosavljevic 2010 [182]	Unclear cohort	n=161, Clinically diagnosed death by neurologic criteria, Missing age	N	N	Y	N	N	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	Not explicitly reported, but reference provided.	Y	M
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
Brasil 2019 [183]	Prospective case control	n=106, Clinically suspected death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	CT-angiography (CTA) – 4 point scale	No26ubarachnoid26 of the internal cerebral veins and M4 middle cerebral arteries bilaterally.	N	M
													Transcranial Doppler (TCD)	Systolic spikes lower than 50cm/sec or nonprogressive oscillatory flow (i.e., diastolic velocity 0 cm/sec or diastolic backflow) were present in the middle cerebral arteries and basilar artery.		
Braun 1997 [184]	Unclear cohort	n=140, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	Y	Y	Y	Four-vessel angiography	Complete absence of hemispheric and posterior fossa circulation, or contrast medium statis within the vertebrobasilar and carotid systems, or persistent and delayed posterior fossa blood flow.	N	< 24 hours
Brunser 2015 [185]	Prospective cohort	n=74, Clinically suspected death by neurologic	N	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	Presence of reverberating, small systolic peaks or the disappearance of a previous flow signal in both middle	N	< 24 hours

		criteria, Adults only												cerebral arteries through the transtemporal window at a depth of 55 mm and through both vertebral arteries identified via insonating through the transforaminal window at a depth of 60 mm.		
Burger 2000 [186]	Unclear cohort	n=21, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	N	N	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion with SPECT	Not explicitly reported, but reference provided.	Y	< 24 hours
													Transcranial Doppler (TCD)	Not explicitly reported, but reference provided.		
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
Calvo 2010 [187]	Unclear cohort	n=13, Clinically diagnosed death by neurologic criteria, Missing age	N	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Radionuclide imaging – HMPAO perfusion without SPECT	Absence of brain perfusion.	Y	M
													Transcranial Doppler (TCD)	Not explicitly reported, but reference provided.		
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
Cao 2013 [188]	Unclear case-control	n=35, Clinically	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	Electroencephalogra	Isoelectric EEG.	Y	M

		suspected death by neurologic criteria, Adults and children											phy (EEG) – Cortical			
Chaparro Hernandez 1984 [189]	Unclear cohort	n=10, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.	Y	M
													Evoked potentials – Brainstem Auditory	Not explicitly reported, but reference provided.		
													Evoked potentials – Visual	Not explicitly reported, but reference provided.		
													Evoked potentials – Somatosensory	Not explicitly reported, but reference provided.		
Chen 1989 [190]	Unclear cohort	n=21, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Electroencephalography (EEG) – Cortical	Isoelectric EEG.	N	< 24 hours
													Evoked potentials – Brainstem Auditory	Absence of all waveforms or the presence of wave-I only.		
Combes 2007 [191]	Prospective cohort	n=43, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – 10 point scale	The criteria diagnosing cerebral circulatory arrest were the nonopacification of the A2 segment of the right and left anterior cerebral artery, M4 segment of the right and left	M	< 24 hours

														middle cerebral artery, P2 segment of the right and left posterior cerebral artery, basilar artery, right and left internal cerebral veins, and finally the great cerebral vein. All the criteria were necessary to establish brain death.		
													Four-vessel angiography	Visualization of cerebral blood flow arrest at the level of the foramen magnum for the posterior circulation and the carotid siphon for the anterior circulation.		
Conti 2009 [192]	Retrospective cohort	n=184, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	Y	N	Y	Transcranial Doppler (TCD)	Cerebral circulatory arrest flow pattern, as per the 2003 working group of the National Commission for Transplant.	N	M
Davalos 1993 [193]	Unclear cohort	n=23, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	N	N	Clinical examination with confirmatory ancillary test	Y	N	Y	N	Transcranial Doppler (TCD)	Not explicitly reported, but reference provided.	N	M
de Freitas 2006 [194]	Prospective cohort	n=270, Clinically diagnosed death by neurologic	Y	Y	Y	Y	Y	Clinical examination	N	N	N	Y	Transcranial Doppler (TCD)	Oscillating flow or short systolic spikes (shorter than 50 cm/s) had to be demonstrated in at least two different	N	≥ 24 hours

		criteria, Adults only												arteries, with the vertebrobasilar artery counting as one artery (e.g. vertebrobasilar artery and one middle cerebral artery, vertebrobasilar artery and one internal carotid artery, both middle cerebral arteries, both internal carotid arteries, or one internal carotid artery plus the contralateral middle cerebral artery) and no signal could be detected in the remaining arteries; absence of flow had to be present for at least 30 min. A lack of signal was not considered proof of cerebral circulatory arrest (CCA), as this finding can be caused by transmission problems. However, disappearance of intracranial flow (lack of signal in patients who had a detectable signal when not in brain death) was accepted as proof of CCA. For the purposes of the present study, and in contrast to the World		

														Federation of Neurology criteria, persistence of isolated flow in the internal carotid arteries with demonstration of CCA in all other intracranial arteries was considered compatible with CCA, as suggested previously. When there was persistence of flow in the internal carotid artery, but no signal in the ipsilateral middle cerebral artery, patients were included in the persistent flow group, as these findings could result from transmission problems, and possible intracranial flow could not be excluded.		
Deseano-Estudillo 2003 [195]	Unclear cohort	n=42, Clinically diagnosed death by neurologic criteria, Adults only	Y	N	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	Y	Y	Y	Transcranial Doppler (TCD)	Flow less than 10 cm/s or reverberant flow in the circle of Willis, internal carotid artery, basilary artery and vertebral arteries.	N	M
Dominguez-Roldan 1995 [196]	Unclear cohort	n=75, Clinically suspected death by neurologic criteria, Adults and children	N	Y	N	N	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	Absence of flow in diastolic-systolic phase; flow reverberating pattern; systolic spikes.	Y	M

Dosemeci 2004 [197]	Unclear cohort	n=100, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	The following flow patterns were regarded as consistent with the TCD diagnosis of brain death: (1) brief systolic forward flow or systolic spikes and diastolic reverse flow, (2) brief systolic forward flow or systolic spikes and no diastolic flow, or (3) no demonstrable flow in a patient in whom flow had been clearly documented in a previous TCD examination. The above TCD findings were only accepted as confirmatory of brain death when they were found bilaterally or in at least three different arteries for at least 3 minutes within the same examination. In patients with a unilateral absent temporal bone window, the finding of typical TCD signals in three different arterial segments on one side was accepted as confirmatory. The finding of diastolic back-and-forward flow (to-and-fro	Y	< 24 hours

														flow) was not considered as confirmatory of brain death, and the examination was repeated until brain death was confirmed ultrasonographically. Absence of flow in all arterial segments during the first TCD examination can be caused by total cerebral circulatory arrest or possibly by the absence of an adequate temporal bone window. All cases in which no flow could be detected at the initial TCD examination were considered as having an absent bone window (missing results).		
Ducrocq 1998 [198]	Retrospective cohort	n=130, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	Transcranial Doppler (TCD)	To-and-fro flow, systolic wave during diastole with or without a continuous diastolic signal (translated from French).	N	M
Dupas 1998 [199]	Prospective case control	n=25, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	Y	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	CT-angiography (CTA) – 7 point scale	Enhanced visibility (i.e. opacification) of the superior ophthalmic veins ... in combination with absence of opacification of the pericallosal artery, terminal arteries for	Y	M

														the cortex, internal cerebral vein, great cerebral vein, and straight sinus.		
Escudero 2009 [200]	Prospective cohort	n=27, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	CT-angiography (CTA) – no intracranial flow	A lack of brain circulation was defined according to the Quality Standards Subcommittee of the American Academy of Neurology, as no intracerebral filling at the level of the carotid bifurcation or circle of Willis. A lack of posterior circulation was indicated by contrast stop at the magnum foramen.	N	< 24 hours
													CT-perfusion (CTP)	A lack of cerebral perfusion was recorded when no blood flow was detected; this is described by the software as an incapacity for automatic postprocessing of information, indicating null cerebral blood flow, cerebral blood volume, and mean transit time.		
													Transcranial Doppler (TCD)	The presence of reverberating flow and systolic spikes was taken to denote cerebral circulatory arrest; the		

														examination was considered complete when the two middle cerebral arteries and posterior circulation at least could be insonated.		
Facco 1998 [201]	Prospective cohort	n=50, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	Y	N	Y	Radionuclide imaging – HMPAO perfusion with SPECT	"Empty skull" perfusion (bone and paranasal sinus perfusion permitted).	N	M
Fages 2004 [202]	Retrospective cohort	n=44, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	N	Clinical examination	N	N	N	Y	Transcranial Doppler (TCD)	No effective flow in 2 or more of the cerebral anterior or medial carotids or in the vertebral and basilar arteries. Flow pattern compatible with cessation of flow included a 2-phase flow with zero net flow and systolic peaks (an acute/narrow unidirectional signal in the early phase of systole of <200 ms duration and average speed <10 cm/s, in the absence of flow in the rest of the cardiac cycle).	N	M
Feri 1994 [203]	Prospective cohort	n=37, Clinically suspected death by neurologic criteria,	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	Following patterns met the criteria for brain death: (1) diastolic reverse flow without diastolic forward	N	M

		Adults and children												flow; (2) brief systolic forward flow; I undetectable flow.		
Fernandez-Torre 2013 [204]	Retrospective cohort	n=329, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Electroencephalography (EEG) – Cortical	The EEG was considered to reflect electrocerebral inactivity when there was no activity above 2 microV for 30 min of recording at a sensitivity of 2 microV per millimeter.	Y	M
Flowers 1997 [205]	Retrospective cohort	n=219, Clinically suspected death by neurologic criteria, Adults and children	NR	NR	NR	NR	NR	Clinical examination	Y	N	N	Y	Radionuclide imaging – Tc-99 pertechnetate angiography	Lack of visualization of cerebral arterial flow after clear demonstration of the carotid arteries. Isolated venous sinus activity was not considered evidence of blood flow adequate to maintain brain viability.	Y	M
Frampas 2009 [206]	Prospective cohort	n=105, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	CT-angiography (CTA) – 4 point scale	Novel 4-point CTA score based on the lack of opacification of cortical segments of the middle cerebral arteries and the 2 internal cerebral veins.	Y	M
													CT-angiography (CTA) – 7 point scale	Following Dupas et al, a point was given for each vessel without opacification (pericallosal arteries, cortical segments of of the		

														middle cerebral arteries, right and left internal cerebral veins, and great cerebral vein), resulting in "lack of opacification" scores of between 0 and 7.		
Friedrich-Borchardt 1988 [207]	Unclear cohort	n=57, Clinically diagnosed death by neurologic criteria, Missing age	N	Y	Y	N	Y	Clinical examination	Y	N	N	Y	Electroencephalography (EEG) – Cortical	Isoelectric EEG.	Y	< 24 hours
Garrel 1984 [208]	Unclear cohort	n=205, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	Y	Y	Clinical examination	Y	Y	N	Y	Electroencephalography (EEG) – Cortical	Inactive/flat line EEG.	Y	M
													Evoked potentials – Brainstem Auditory	Disappearance of auditory evoked potentials signalled brain death, in the absence of bilateral deafness.		
Garrett 2018 [209]	Prospective cohort	n=18, Clinically suspected death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	CT-angiography (CTA) – 4 point scale	Absence of flow in the bilateral cortical middle cerebral arteries (M2) and bilateral internal cerebral veins.	M	< 24 hours
Goodman 1985 [210]	Retrospective cohort	n=204, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Radionuclide imaging – other	Complete absence of all arterial and venous flow on the dynamic study as well as nonvisualization of dural sinuses on the static scan.	Y	< 24 hours
	Unclear cohort	n=56, Clinically	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	Radionuclide	No cerebral perfusion.	Y	M

Grigg 1987 [211]		diagnosed death by neurologic criteria, Adults and children											imaging – Tc-99 pertechnetate angiography			
													Electroencephalography (EEG) – Cortical	Electrocortical silence for 30 minutes.		
Hadani 1999 [212]	Unclear cohort	n=137, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	The presence of such TCD patterns as an oscillating flow pattern with a negative diastolic component and short systolic spikes were considered to be specific for the circulatory arrest. The results of TCD examination in the present study were regarded as confirmatory of total cerebral circulatory arrest if they conformed to the following preset conditions: (1) the above-mentioned specific TCD patterns were present bilaterally in the internal carotid arteries, middle cerebral arteries, vertebral arteries and basilar artery within the same examination; (2) absence of a signal from a vessel was regarded as a sign	N	M

														of flow cessation only if typical TCD patterns were seen in other vessels within the same examination, or if a previous TCD examination had detected a clear signal from the vessel in patients who were examined more than once; (3) signals with stable wave forms, typical for circulatory arrest, were recorded from each examined vessel for at least 3 min and the total duration of the TCD examination was a minimum 30 min.		
Hashemian 2016 [213]	Unclear cohort	n=35, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	Y	Y	Y	Transcranial Doppler (TCD)	Oscillating flow or systolic spikes in addition to reversed diastolic flow were considered as indicatives of brain death.	M	M
Hassler 1989 [214]	Unclear cohort	n=65, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	Four-vessel angiography	Intracranial arterial filling was considered evidence of intracranial circulatory arrest when the tapering column of contrast medium terminated in the39ubarachnoid arterial segments without subsequent orthograde drainage and venous	Y	M

														enhancement after 26 seconds. In accordance with the suggestion of Kricheff et al., this was termed subarachnoid arterial "stasis filling".		
													Transcranial Doppler (TCD)	Circulatory arrest in the anterior and posterior intracranial circulation by the presence of one of the three flow velocity pattern types: oscillating flow, systolic spike, zero flow (absence of TCD signals diagnosed by repeated TCD examinations when signals have disappeared from the vessel).		
Haupt 1991 [215]	Unclear cohort	n=82, Clinically diagnosed death by neurologic criteria, Missing age	N	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Evoked potentials – Brainstem Auditory	No intracerebral stimulus response components (Wave III-V) were detectable (translated from German).	Y	M
Hernandez-Hernandez 2019 [216]	Retrospective cohort	n=447, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	N	Y	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 4 point scale	Four-vessel CTA criteria (as per Frampas et al.)	Y	< 24 hours
													CT-angiography (CTA) – no	Absence of intracranial flow.		

													intracranial flow			
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
Hicks 1979 [217]	Unclear case-control	n=42, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	N	Electroencephalography (EEG) – Cortical	Isoelectric EEG.	Y	M
Hoffmann 2015 [218]	Retrospective cohort	n=1419, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	Four-vessel angiography	Not explicitly reported, but reference provided.	Y	≥ 24 hours
													Radionuclide imaging – other	Absence of perfusion on a brain nuclear scan.		
													Transcranial Doppler (TCD)	Demonstration of oscillating flow or short systolic spikes in the carotid, vertebral, basilar, and basal cerebral arteries on extracranial and transcranial Doppler ultrasound.		
													Electroencephalography (EEG) – Cortical	Silent EEG (30 minutes).		
													Evoked potentials – Somatosensory	Interruption of median nerve sensory evoked potentials at the level of the second cervical vertebra.		

Holeckova2014 [219]	Retrospective cohort	n=41, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Evoked potentials – Brainstem Auditory	Absence of waves III-V.	N	M
													Evoked potentials – Somatosensory	Absence of peaks P14/N18 and N20.		
Huttemann 2000 [220]	Prospective cohort	n=45, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	Y	Y	Clinical examination	Y	N	N	N	Transcranial Doppler (TCD)	Oscillatory pattern, systolic spikes, or zero flow.	M	M
Jorgensen 1973 [221]	Unclear cohort	n=42, Clinically diagnosed death by neurologic criteria, Missing age	N	Y	N	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	Y	N	Four-vessel angiography	Absence of cerebral circulation.	Y	< 24 hours
Kahveci 2002 [222]	Unclear cohort	n=15, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion with SPECT	Empty skull: no uptake of Tc-99m HMPAO in the cerebrum, cerebellum and brainstem.	Y	M
Kang 2015 [223]	Case series	n=5, Clinically diagnosed death by neurologic criteria, Adults only	Y	N	N	Y	Y	Clinical examination	Y	Y	Y	Y	Magnetic resonance perfusion (MRP) – Arterial spin labeling	1) Extremely decreased perfusion in the whole brain, 2) Bright vessel signal intensity around the entry of the carotid artery to the skull suggesting flow stagnation, and 3) Patent external carotid circulation	N	≥ 24 hours

														corresponding to the findings of brain death on conventional angiography.		
Karakus 2014 [224]	Retrospective cohort	n=14, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – 4 point scale	Four-point scoring method in which opacification loss in cortical segments of middle cerebral arteries and two internal cerebral veins are studied developed by Frampas et al was used for evaluation.	N	M
Karantanas 2002 [225]	Prospective case control	n=30, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination	Y	Y	Y	Y	Magnetic resonance imaging (MRI) – Time of flight (TOF)	No arterial intracranial circulation.	Y	< 24 hours
													Magnetic resonance veinography (MRV)	No venous intracranial flow.		
Kato 1991 [226]	Unclear cohort	n=24, Clinically diagnosed death by neurologic criteria, Adults and children	Y	N	Y	N	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Magnetic resonance imaging (MRI) – Other	Lack of seven peaks observable in healthy brains (PME, Pi, phosphodiester (PDE), PCr, y-ATP, alpha-ATP, and beta-ATP). A high monopeak (Pi peak that included PDE with a high and wide bottom) was observed in a majority of clinically brain dead patients.	Y	M

Keller 1981 [227]	Unclear cohort	n=25, Clinically diagnosed death by neurologic criteria, Missing age	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Cessation of cerebral blood flow in the internal carotid arteries (translated from German).	Y	M
Kerhuel 2016 [228]	Retrospective cohort	n=104, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – other criteria	Circulatory cerebral arrest according to the seven-score (Dupas et al) or the four-score (Frampas et al) scales.	N	< 24 hours
Kramar 2001 [229]	Unclear cohort	n=40, Clinically diagnosed death by neurologic criteria, Missing age	NR	NR	NR	NR	NR	Clinical examination	Y	Y	Y	Y	Four-vessel angiography	Not explicitly reported, but reference provided.	N	M
													Transcranial Doppler (TCD)	If at least one of the 4 measured blood vessels (middle cerebral arteries (2) and vertebral arteries (2) OR transorbital carotid siphons (2) and vertebral arteries (2)) demonstrated preservation of flow, the diagnosis of brain death was excluded. If no signal could be captured from one of the vessels, the test was inconclusive. If all 4 vessels were evaluable and demonstrated absence of perfusion, brain death was		

														considered confirmed.		
Kuni 1985 [230]	Retrospective cohort	n=35, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	Radionuclide imaging – Tc-99 pertechnetate angiography	Absence of intracranial perfusion, and usually the absence of superior sagittal sinus radioactivity on the high count-density image.	Y	M
Kuo 2006 [231]	Unclear cohort	n=101, Clinically suspected death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	Transcranial Doppler (TCD)	The presence of a specific TCD flow pattern, such as a reverse diastolic flow, a very small systolic spike, or no signal, as described by Ducrocq et al in both the middle cerebral arteries and basilar artery.	Y	M
Kurtek 2000 [232]	Unclear cohort	n=23, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	N	N	Y	Clinical examination with confirmatory ancillary test	Y	Y	N	Y	Radionuclide imaging – HMPAO perfusion without SPECT	No cerebral perfusion.	N	M
Kwiecinksi 1994 [233]	Unclear cohort	n=20, Clinically diagnosed death by neurologic criteria, Adults only	N	N	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Changes in flow in cerebral arteries described by Petty et al (translated from Polish).	Y	M
													Electroencephalography (EEG) – Cortical	Isoelectric EEG (translated from Polish).		
Lampl 2002 [234]	Prospective cohort	n=57, Clinically diagnosed death by neurologic	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Oscillatory flow or systolic spikes in any cerebral artery which can be recorded by bilateral transcranial	N	M

		criteria, Adults only												insonation of internal carotid arteries and middle cerebral arteries, and any branch of other artery which can be recorded (anterior and posterior circulation).		
Laurin 1989 [235]	Retrospective cohort	n=26, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion with SPECT	The planar images were interpreted as consistent with brain death if no uptake of [99mTc]HM-PAO was seen in either the cerebrum or the cerebellum.	Y	M
													Radionuclide imaging – Tc-99 HMPAO angiography	No arterial flow was observed in the major intracranial arteries.		
Lemmon 1995 [236]	Retrospective cohort	n=24, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	N	Y	N	Clinical examination	Y	Y	Y	Y	Radionuclide imaging – other	No cerebral blood flow.	Y	M
													Transcranial Doppler (TCD)	No cerebral blood flow.		
Li 2016 [237]	Retrospective cohort	n=42, Clinically suspected death by neurologic criteria, Adults only	N	Y	N	N	Y	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Oscillating waveform and sharp spikes or peaks waveforms.	M	M
Link 1988 [238]	Unclear cohort	n=41, Clinically suspected	NR	NR	NR	NR	NR	Four-vessel angiography	N/A	N/A	N/A	N/A	Radionuclide imaging –	No cerebral perfusion (translated from German).	N	M

		death by neurologic criteria, Missing age											Tc-99 pertechnetate angiography			
													Evoked potentials – Brainstem Auditory	One of the following: (1) No derived potentials, (2) Wave I unilaterally, (3) Wave I bilaterally, (4) Wave I and II either unilateral or bilateral (translated from German).		
Lopez-Navidad 2000 [239]	Prospective cohort	n=36, Clinically diagnosed death by neurologic criteria, Adults and children	NR	NR	NR	NR	NR	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion without SPECT	No perfusion of supra and infratentorial encephalic structures.	N	≥ 24 hours
													Transcranial Doppler (TCD)	Criteria of the Federal Organization of the German Medical Council; i.e., oscillating flow or short systolic spike pattern recorded in at least two intracranial arteries corresponding to different hemispheres.		
Lovrencic-Huzjan 2011 [240]	Case series	n=40, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	Y	N	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – no intracranial flow	Lack of opacification of any intracranial blood flow.	Y	≥ 24 hours
													Four-vessel	Stop of the contrast at the scull base, after the iodinated		

													angiography	contrast medium is injected under high pressure in both the anterior and the posterior circulation.		
													Radionuclide imaging – other	Absence of cerebral flow on anterior-projection rapid sequence angiography, obtained for up to 1 minute intravenous bolus injection of the radiopharmaceutical.		
													Transcranial Doppler (TCD)	The following extra and intracranial Doppler sonographic findings have been recorded and documented both intra- and extracranially and bilaterally in two examinations at an interval of at least 30 mins: systolic spikes or oscillating flow in any cerebral artery (at least one middle cerebral artery at one temporal bone window), recorded by bilateral transcranial insonation for anterior circulation, and any intracranial vertebral or basilar artery which is recorded by sub-		

														occipital insonation for the posterior circulation...The diagnosis established by the intracranial examination must be confirmed by extracranial bilateral recording of the common carotid arteries, internal carotid arteries and vertebral arteries.		
Luo 2006 [241]	Unclear cohort	n=88, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Electroencephalography (EEG) – Cortical	Electrical silence with brain waves lower than 2 microV (translated from Chinese).	Y	≥ 24 hours
Luo 2005 [242]	Unclear cohort	n=95, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	N	N	N	N	Evoked potentials – Somatosensory	N20-P25 potentials and N18 potential both disappear (translated from Chinese).	N	M
Macdonald 2018 [243]	Retrospective cohort	n=74, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – 4 point scale CT-angiography (CTA) – 7 point scale	Contrast opacification was assessed as a binary outcome of yes/no for extracranial vessels, intracranial internal carotid artery (supraclinoid), middle cerebral artery branches (M1, M2), anterior cerebral artery branches (A1, A2),	Y	≥ 24 hours

													CT-angiography (CTA) – 10 point scale	intracranial vertebral artery, intracranial basilar artery, internal cerebral vein, and vein of Galen. CTA was assessed on 4-point, 7-point, and 10-point scales, as per Frampas et al, Dupas et al, and Combes et al.		
													CT-perfusion (CTP)	Appearance and subsequent disappearance of contrast media in superficial scalp vessels (eg, superficial temporal artery branches) to establish successful intravascular injection of the contrast, as well as complete coverage of a cardiac cycle. Marked-matched decrease of cerebral blood flow (CBF) and cerebral blood volume (CBV) in the whole brain, in the brainstem, and isolated brain stem defect (matched defect on CBF and CBV in the brainstem but preservation in the rest of the brain) were recorded.		

													Radionuclide imaging – HMPAO perfusion without SPECT	No tracer activity was recorded when a "hollow skull/empty light bulb" sign was seen.		
Marchand 2016 [244]	Unclear cohort	n=76, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	Y	Y	Clinical examination	N	N	N	Y	CT-angiography (CTA) – 4 point scale	Non-opacification of the cortical segment of each middle cerebral artery and the non-opacification of each internal cortical vein.	Y	M
													CT-angiography (CTA) – other criteria	Non-opacification of both the internal cerebral veins and infratentorial superior petrosal vein.		
Matsumura 1996 [245]	Unclear cohort	n=15, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	N	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Four-vessel angiography	Absence of cerebral blood flow as the non-filling phenomenon in both carotid and vertebral arteries.	Y	M
													Magnetic resonance imaging (MRI) – Time of flight (TOF)	Disappearance of flow void or flow void patterns as spotty area in the cavernous internal carotid arteries as well as middle cerebral arteries or anterior cerebral arteries.		
McPeck 1981 [246]	Unclear cohort	n=10, Clinically diagnosed death by neurologic criteria,	Y	Y	Y	N	Y	Clinical examination	N	N	N	Y	Electroencephalography (EEG) – Cortical	Isoelectric EEG.	N	M

		Adults and children														
Mendez 1983 [247]	Unclear cohort	n=15, Clinically diagnosed death by neurologic criteria, Missing age	NR	NR	NR	NR	NR	Clinical examination	Y	Y	Y	Y	Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.	N	M
Migdady 2021 [248]	Retrospective cohort	n=8, Clinically diagnosed death by neurologic criteria, Adults only	Y	N	Y	Y	N	Clinical examination	Y	Y	Y	Y	Transcranial Doppler (TCD)	Pattern of cerebral circulatory arrest (small systolic peaks with absent diastolic flow or a reverberating flow pattern in anterior and posterior circulation); if no flow was seen, the test was considered inconclusive.	M	M
Moya Sanchez 2020 [249]	Prospective cohort	n=56, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	N	Clinical examination	NR	NR	NR	NR	Radionuclide imaging – HMPAO perfusion without SPECT	Absence of perfusion in the cerebral hemispheres and posterior fossa (‘‘hollow skull’’ sign).	M	< 24 hours
													Transcranial Doppler (TCD)	Presence of inverted diastolic flow and systolic spikes.		
													Electroencephalography (EEG) – Cortical	Not explicitly reported, but reference provided.		
Mrhac 1995 [250]	Retrospective cohort	n=54, Clinically suspected death by neurologic criteria, Adults and children	NR	NR	NR	NR	NR	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion without SPECT	Qualitative visual assessment, three-pronged fork, hollow skull, hot nose, blood flow index, delayed uptake index.	Y	M

Munari 2005 [251]	Prospective cohort	n=20, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	Y	Clinical examination	Y	Y	N	Y	Four-vessel angiography	(a) Absent filling of the intracranial arteries at the entry into the skull (at the foramen magnum in the posterior circulation and at the petrosal portion of the carotid artery in the anterior circulation); (b) Minimal arterial opacification with absent parenchymal and venous phases.	N	M
													Radionuclide imaging – HMPAO perfusion with SPECT	Empty skull (i.e., absent perfusion of all supra- and infratentorial encephalic structures).		
Nau 1992 [252]	Unclear cohort	n=50, Clinically diagnosed death by neurologic criteria, Adults only	Y	N	Y	Y	Y	Clinical examination	Y	N	Y	Y	Four-vessel angiography	Contrast medium in the vertebrobasilary system could not pass the atlantooccipital joint; in the carotid arteries contrast medium up to but not beyond the branching of the ophthalmic artery was accepted. Contrast medium had to be clearly visible in the external carotid arteries and their branches.	N	≥ 24 hours
													Transcranial Doppler (TCD)	A systolic flow followed by a reversal of flow during diastole		

														(oscillating flow) as well as a sharp small peak at the beginning of the systole and a zero flow velocity during the rest of the cardiac cycle (“systolic spikes”) in both carotid and both vertebral arteries were considered typical for cessation of cerebral blood flow. A relatively high systolic flow velocity and no flow at the end of diastole (“systolic peaks”, or a mixed pattern of oscillating flow or “systolic spikes” in one or more brain-supplying extracranial arteries and “systolic peaks” in the remaining arteries was deemed suggestive of intracranial circulatory arrest.		
													Electroencephalography (EEG) – Cortical	Isoelectric EEG.		
													Evoked potentials – Brainstem Auditory	Loss of waves III-V, II-V or no reproducible brainstem auditory evoked potentials on both sides.		

Nebra 2001 [253]	Unclear cohort	n=25, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	N	N	Clinical examination	Y	Y	N	Y	Transcranial Doppler (TCD)	Any of the following patterns in both the infra- and supratentorial regions supported the diagnosis of brain death: (a) a reverberant pattern; (b) a pattern of isolated or spiculated systolic peaks; (c) an absence of signal, where blood flow existed on a previous TCD.	Y	M
Newberg 2002 [254]	Retrospective cohort	n=58, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	N	Y	N	Clinical examination	Y	N	N	Y	Radionuclide imaging – Tc-99 HMPAO angiography	Complete absence of flow throughout the brain and the internal carotid arteries.	N	M
Newell 1989 [255]	Unclear cohort	n=12, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	N	N	Clinical examination	Y	N	N	Y	Radionuclide imaging – other	Absence of intracerebral arterial and venous sinus flow on the dynamic images, as well as absence of venous sinus activity on the static image.	Y	M
													Transcranial Doppler (TCD)	Reverberating flow with forward flow in systole and retrograde flow in diastole.		
Nunes 2019 [256]	Unclear case-control	n=70, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	CT-angiography (CTA) – 4 point scale	Four-point scale (as per Frampas et al).	Y	< 24 hours
													CT-angiography (CTA)	Absence of opacification of the M4 branches in the		

													– other criteria	arterial phase and internal carotid arteries in the venous phase.		
Okii 1996 [257]	Unclear case-control	n=29, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Electroencephalography (EEG) – Cortical	Flat scalp EEG.	Y	M
													Electroencephalography (EEG) – Nasopharyngeal	Not explicitly reported, but reference provided.		
Oleschko Arruda 1987 [258]	Retrospective cohort	n=33, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	Electroencephalography (EEG) – Cortical	Absence of brain activity above 2 microvolts in all areas of the head (isoelectric EEG).	N	M
Olumunun 1997 [259]	Unclear cohort	n=29, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	N	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	Either absent or reversed diastolic flow or small early systolic spikes.	Y	< 24 hours
Pagola 2010 [260]	Prospective cohort	n=142, Clinically diagnosed death by neurologic criteria, Missing age	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Reverberant flow, isolated systolic spike, or flow absence if it was previously recorded.	Y	M
Paolin 1995 [261]	Prospective cohort	n=15, Clinically diagnosed death by	N	Y	Y	N	Y	Clinical examination	Y	N	N	Y	Four-vessel angiography	Not explicitly reported, but reference provided.	N	M

		neurologic criteria, Adults only											Transcranial Doppler (TCD)	Oscillating flow or systolic spikes.		
													Electroencephalography (EEG) – Cortical	Electrocerebral silence.		
													Xenon-CT	Not explicitly reported, but reference provided.		
Patel 1988 [262]	Unclear cohort	n=14, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	Y	Y	Y	Radionuclide imaging – Tc-99 DTPA angiography	Absence of intracranial arterial perfusion and the absence of superior sagittal sinus activity on the dynamic and static images. Presence of sagittal sinus activity in the absence of intracranial arterial flow was considered indeterminate for the evidence of brain death.	Y	M
Payen 1990 [263]	Prospective case control	n=28, Clinically suspected death by neurologic criteria, Adults only	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	Value of Qed (blood flow) of less than 31.4 ml/mn.	N	M
Pedicelli 2019 [264]	Retrospective cohort	n=123, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	N	N	Clinical examination	NR	NR	NR	NR	CT-angiography (CTA) – no intracranial flow	Lack of brain circulation.	M	M
													Four-vessel angiography	Absence of filling of intracranial arteries at the level		

														of their subarachnoid entry.		
													Transcranial Doppler (TCD)	Oscillating flow, systolic spikes, or no flow signal.		
													Other	Oscillating flow, systolic spikes, or no flow signal.		
Petty 1990 [265]	Unclear cohort	n=54, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	N	N	N	Y	Transcranial Doppler (TCD)	TCD high-resistance waveform abnormality, consisting of either absent or reversed diastolic flow, or small early systolic spikes.	N	M
Picard 1995 [266]	Unclear cohort	n=125, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Four-vessel angiography	Absence of cerebral blood flow.	N	< 24 hours
Pistoia 1991 [267]	Retrospective cohort	n=30, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination	Y	N	N	N	Xenon-CT	Global flow values of less than 5 ml/100 ml/min.	Y	M
Poularas 2006 [268]	Unclear cohort	n=40, Clinically diagnosed death by neurologic criteria, Missing age	N	Y	Y	Y	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	(1) Brief systolic forward flow or systolic spikes and diastolic reversed flow, or (2) Brief systolic forward flow or systolic spikes and no diastolic flow, or (3) No demonstrable flow in a patient in	Y	< 24 hours

														whom flow had been clearly documented in a previous TCD examination.		
Powers 1989 [269]	Unclear cohort	n=24, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	Y	Y	Y	Transcranial Doppler (TCD)	Early changes were decreased flow velocity as well as increased pulse pressure. Late changes were persistent increase in pulse pressure with appearance of retrograde flow velocities during diastole. In the end, complete diastolic retrograde flow velocities that gave rise to characteristic reverberating pattern.	Y	M
Quesnel 2007 [270]	Prospective cohort	n=21, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	CT-angiography (CTA) – 7 point scale	Lack of opacification of seven cerebral vessels: the left and right pericallosal arteries (1 point each), the left and right terminal arteries of the cortex (1 point each), the left and right internal cerebral veins (1 point each), and the great cerebral vein (1 point).	N	< 24 hours
Rao 2009 [271]	Unclear cohort	n=50, Clinically diagnosed death by neurologic	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Mean flow velocity of 10-15 cm/sec or less with either reverberating, forward or	Y	M

		criteria, Adults only												backward flow or only systolic flow with no diastolic flow.		
Rieke 2011 [272]	Retrospective cohort	n=29, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	N	N	N	Y	CT-angiography (CTA) – 4 point scale CT-angiography (CTA) – 7 point scale	Two criteria were used to determine circulatory arrest according to CT angio and venous-phase CT. For Dupas criteria, circulatory arrest was defined by non-opacification of 7 regions [terminal braches (M4) of the right middle cerebral artery; terminal braches (M4) of the left middle cerebral artery; right pericallosal artery (A3); left pericallosal artery (A3); right internal cerebral vein; left internal cerebral vein; great cerebral vein]. The Frampas criteria evaluated non-opacification of four regions [terminal braches (M4) of the right middle cerebral artery; terminal braches (M4) of the left middle cerebral artery; right internal cerebral vein; left internal cerebral vein].	Y	M

Ropper 1987 [273]	Unclear cohort	n=24, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	N	N	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	Brief, sharply contoured systolic envelope with reversal of flow during diastole.	N	< 24 hours
Rosendahl 1994 [274]	Case series	n=15, Clinically suspected death by neurologic criteria, Adults only	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	N	Y	Y	Transcranial Doppler (TCD)	Resistive cerebral arterial flow (i.e., no flow), no antegrade diastolic flow.	Y	M
Sahin 2015 [275]	Retrospective cohort	n=25, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	Y	N	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 4 point scale CT-angiography (CTA) – 7 point scale CT-angiography (CTA) – 10 point scale	Diagnosis of brain death was assessed according to the previously established 10-, 7-, and 4-point scoring systems in CT angiography (as per Combes et al, Dupas et al, Frampas et al).	Y	≥ 24 hours
Sanjeev 2011 [276]	Unclear cohort	n=152, Clinically diagnosed death by neurologic criteria, Adults only	NR	NR	NR	NR	NR	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Small systolic flow, absence of diastolic filling, reversal of flow during diastole and reverberating flow pattern in the major arterial trunks of the Circle of Willis.	Y	< 24 hours
Sawicki 2015 [277]	Prospective cohort	n=84, Clinically diagnosed death by neurologic	Y	Y	Y	Y	N	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 10 point scale	No61pacification of the following vessels is noted in the 60-second phase: anterior cerebral arteries-A3,	Y	M

		criteria, Adults only											middle cerebral arteries-M4, posterior cerebral arteries-P2, basilar artery, internal cerebral veins and great cerebral vein.			
													CT-angiography (CTA) – other criteria	No62pacification of the following vessels is noted in the 25-second phase: anterior cerebral arteries-A3, middle cerebral arteries-M4, posterior cerebral arteries-P2, basilar artery, internal cerebral veins and great cerebral vein.		
													Four-vessel angiography	No filling of bilateral internal carotid arteries beyond level of the anterior clinoid process and bilateral vertebral arteries beyond their dural penetration and the internal cerebral veins, or Stasis filling defined as delayed and persistent opacification of the circle of Willis without opacification of the cortical arterial branches, visualization of parenchymal phase or deep venous outflow.		

Sawicki 2018 [278]	Prospective case control	n=55, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	N	N	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 4 point scale	Four-point scale based on the lack of opacification of the cortical segments of the middle cerebral arteries and the 2 internal cerebral veins.	M	M
Sawicki 2019 [279]	Prospective cohort	n=50, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	N	N	Y	Clinical examination	Y	Y	Y	Y	CT-perfusion (CTP)	Cerebral blood flow and/or cerebral blood volume values in any region of interest below 10 mL/100 g/min and 1.0 mL/100 g, respectively.	N	M
Schlake 1992 [280]	Unclear cohort	n=24, Clinically suspected death by neurologic criteria, Adults and children	Y	N	Y	Y	Y	Clinical examination	Y	N	N	Y	Radionuclide imaging – HMPAO perfusion without SPECT	Cessation of either cerebral or cerebellar perfusion.	N	< 24 hours
													Electroencephalography (EEG) – Cortical	Electrocortical silence.		
													Evoked potentials – Brainstem Auditory	Not explicitly reported, but reference provided.		
													Evoked potentials – Somatosensory	Not explicitly reported, but reference provided.		
Shankar 2013 [281]	Retrospective cohort	n=11, Clinically diagnosed death by neurologic	Y	N	Y	N	Y	Clinical examination	Y	N	N	Y	CT-angiography (CTA) – 4 point scale	Intracranial non-opacification based on 4- and 7-point scales (as per	N	M

		criteria, Adults only											CT-angiography (CTA) - 7 point scale	Frampas et al and Dupas et al).		
													CT-perfusion (CTP)	Either no or a matched decrease in cerebral blood flow and cerebral blood volume in the brainstem.		
Sheikh 2008 [282]	Prospective cohort	n=40, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	High-resistance waveform abnormality of to-and-fro TCD pattern flow (consisted of systolic antegrade flow and diastolic retrograde flow).	N	M
Shukla 1987 [283]	Unclear cohort	n=6, Clinically diagnosed death by neurologic criteria, Missing age	Y	N	N	N	N	Clinical examination	NR	NR	NR	NR	Electroencephalography (EEG) - Cortical	No evidence of electrical activity.	Y	M
													Electroencephalography (EEG) - Nasopharyngeal	No evidence of electrical activity.		
Sohn 2012 [284]	Retrospective case control	n=17, Clinically suspected death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Magnetic resonance imaging (MRI) - Diffusion weighted imaging and apparent diffusion coefficient (DWI/ADC)	Tonsillar herniation; absent intracranial vascular flow void in both conventional MRI and MRA; diffuse cortical high signal intensity and swelling of the cerebral sulci on T2-weighted imaging; diffuse hemispheric hyperintensities on diffusion-weighted	N	M

														imaging; and a drop in the apparent diffusion coefficient due to cytotoxic edema.		
Soldatos 2009 [285]	Unclear cohort	n=76, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	N	Clinical examination	NR	NR	NR	NR	Four-vessel angiography	Absence of filling of intracranial arteries.	Y	M
													Transcranial Doppler (TCD)	Systolic spikes, oscillatory flow or the absence of flow if flow had been documented on a previous examination.		
Srari 2020 [286]	Retrospective cohort	N=66, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – 4 point scale	No opacification in the M4 segments of the middle cerebral arteries and the deep cerebral veins	Y	< 24 hours
													CT-angiography (CTA) – other	Toulouse score, venous score and revised 7-point score		
Stohr 1987 [287]	Unclear cohort	n=20, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Evoked potentials - Somatosensory	Not explicitly reported, but reference provided.	Y	≥ 24 hours
Su 2014 [288]	Prospective cohort	n=131, Clinically suspected death by neurologic criteria, Adults only	Y	N	N	N	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	No cerebral blood flow.	N	M
													Electroencephalography (EEG) - Cortical	Isoelectric EEG.		
													Evoked potentials -	Waves disappear other than waves I.		

													Somatosensory			
Suarez-Kelly 2015 [289]	Prospective case control	n=80, Clinically suspected death by neurologic criteria, Adults only	Y	Y	Y	Y	Y	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) - other criteria	No flow in the middle cerebral arteries-M1, anterior cerebral arteries-A1, and the basilar artery.	N	M
													Radionuclide imaging - Tc-99 DTPA angiography	No intracranial radiotracer uptake manifesting as absent ‘‘trident sign.’’ Presence of trident sign indicates cerebral blood flow consisting of middle cerebral arteries and paired anterior cerebral arteries. The presence of ‘‘hot nose sign,’’ caused by shunting of radiotracer to the external carotid circulation from the internal carotid circulation due to the functional occlusion of the internal carotid by increased intracranial pressure, was also used as an indicator of brain death. On blood pool phase, the radiotracer activity is no longer identified in the vessels, and faint activity is seen within the brain parenchyma. In brain death patients,		

														no parenchymal uptake is evident.		
Tali 2001 [290]	Unclear cohort	n=11, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	NR	NR	NR	NR	Radionuclide imaging - HMPAO perfusion with SPECT	No cortical uptake.	N	M
													Radionuclide imaging - Tc-99 HMPAO angiography	No evidence of intracerebral blood flow.		
													Electroencephalography (EEG) - Cortical	Electrocerebral silence.		
													Magnetic resonance imaging (MRI) - Time of flight (TOF)	Not explicitly reported, but reference provided.		
Tan 1987 [291]	Case series	n=5, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	N	N	Clinical examination	Y	N	N	Y	CT-angiography (CTA) – no intracranial flow	Absence of intracranial blood flow.	Y	M
													Four-vessel angiography	Absence of any intracranial flow.		
													Radionuclide imaging - other	Absence of intracranial circulation.		

Tavakoli 2012 [292]	Retrospective cohort	n=89, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	N	Y	Y	Clinical examination	N	N	N	Y	Electroencephalography (EEG) - Cortical	Electrocerebral silence.	Y	M
Tekeli 2021 [293]	Retrospective cohort	N=22, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	N	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) – No intracranial flow	Contrast enhancement was observed in the common carotid artery and its branches. The absence of a transition to the V4 segment of the vertebral artery, to the basilar artery, to the posterior cerebral artery, and to both the middle cerebral and anterior cerebral arteries were evaluated as compatible with brain death.	N	≥ 24 hours
Vakilian 2012 [294]	Unclear cohort	n=30, Clinically diagnosed death by neurologic criteria, Missing age	Y	Y	Y	Y	Y	Clinical examination with confirmatory ancillary test	Y	N	N	Y	Transcranial Doppler (TCD)	Sonographic patterns constituting cerebral circulatory arrest: (1) systolic spike pattern (without diastolic flow), (2) reverberating flow pattern (brief systolic forward flow and diastolic reverse flow), (3) diastole-systole separation pattern (systolic forward spike flow and diastolic flow with	N	≥ 24 hours

														separation), and (4) no flow pattern.		
Van Bunnen 1989 [295]	Unclear cohort	n=110, Clinically diagnosed death by neurologic criteria, Adults and children	N	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Four-vessel angiography	Cessation of intracranial blood flow.	Y	M
Van Velthoven 1988 [296]	Unclear cohort	n=29, Clinically suspected death by neurologic criteria, Adults and children	N	Y	Y	N	Y	Clinical examination	Y	N	N	Y	Four-vessel angiography	Total stop of brain circulation.	Y	M
													Transcranial Doppler (TCD)	Reverberating flow pattern with counterbalancing forward and backward components of the blood column indicating flow arrest.		
													Electroencephalography (EEG) - Cortical	Isoelectric EEG.		
Vatne 1985 [297]	Unclear cohort	n=7, Clinically diagnosed death by neurologic criteria, Adults only	N	Y	Y	Y	N	Clinical examination	Y	N	N	N	Four-vessel angiography	Cessation of intracranial circulation.	Y	M
Vincenzini 2010 [298]	Case series	n=5, Clinically diagnosed death by neurologic criteria, Adults and children	N	N	N	N	Y	Clinical examination with confirmatory ancillary test	NR	NR	NR	NR	Transcranial Doppler (TCD)	Reverberating flow pattern.	Y	M

Wang 2008 [299]	Unclear cohort	n=111, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	Y	Y	Clinical examination	Y	N	N	Y	Transcranial Doppler (TCD)	Systolic peaks, an oscillating or reverberating flow pattern, or an absence of systolic flow.	N	M
													Electroencephalography (EEG) - Cortical	Wave amplitude < 2 microV.		
													Evoked potentials - Somatosensory	No potential beyond P13.		
Welscheold 2013a [300]	Retrospective cohort	n=102, Clinically diagnosed death by neurologic criteria, Adults and children	Y	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Transcranial Doppler (TCD)	Supratentorial vasculature was assessed through transtemporal, posterior fossa through suboccipital window. Intracranial circulatory arrest was defined according to previously published guidelines.	N	M
Welscheold 2013b [301]	Prospective cohort	n=63, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	Y	N	Clinical examination	Y	Y	Y	Y	CT-angiography (CTA) - 10 point scale	Ten-point scale (as per Combes et al).	N	< 24 hours
													Electroencephalography (EEG) - Cortical	Electrocerebral inactivity.		
Werner 1990 [302]	Unclear cohort	n=47, Clinically suspected death by	Y	Y	Y	N	N	Clinical examination with confirmator	Y	N	N	N	Transcranial Doppler (TCD)	Cerebral circulatory arrest was detected either by bidirectional	Y	M

		neurologic criteria, Adults only						y ancillary test						Doppler signals indicating counterbalancing anterograde and retrograde movements of the blood column or by low anterograde systolic spikes without diastolic flow.		
Wieler 1993 [303]	Unclear cohort	n=16, Clinically diagnosed death by neurologic criteria, Adults only	Y	Y	Y	N	Y	Clinical examination	NR	NR	NR	NR	Four-vessel angiography	No cerebral blood flow.	Y	M
													Radionuclide imaging - HMPAO perfusion with SPECT	No uptake of Tc-99m HMPAO seen in both the cerebrum and cerebellum.		
													Electroencephalography (EEG) - Cortical	Electrocerebral silence.		
Yararbas 2011 [304]	Retrospective cohort	n=24, Clinically diagnosed death by neurologic criteria, Adults and children	N	N	Y	N	Y	Clinical examination	N	N	N	Y	Radionuclide imaging - HMPAO perfusion with SPECT	Absence of Tc99m-HMPAO uptake in cerebral and cerebellar cortexes.	Y	M
													Radionuclide imaging - Tc-99 HMPAO angiography	Absence of perfusion in anterior and medial cerebral arteries, sinus activity in sagittal and transverse sinuses.		
Ying 1992 [305]	Unclear case-control	n=26, Clinically suspected	Y	Y	N	Y	N	Clinical examination	Y	N	N	N	Evoked potentials -	Cortical N20 waves bilaterally absent.	N	≥ 24 hours

		death by neurologic criteria, Adults and children											Somatosensory			
Zhang 2008 [306]	Unclear cohort	n=35, Clinically suspected death by neurologic criteria, Adults and children	Y	N	Y	Y	Y	Clinical examination	Y	N	N	Y	Electroencephalography (EEG) - Cortical	Isoelectric EEG.	Y	M

Legend:

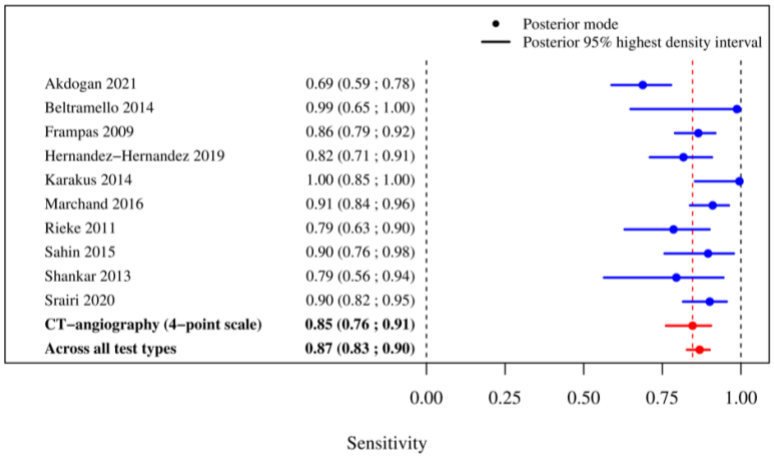
DNC = death determination by neurologic criteria

Y = yes, N = no, M = missing, NR = not reported

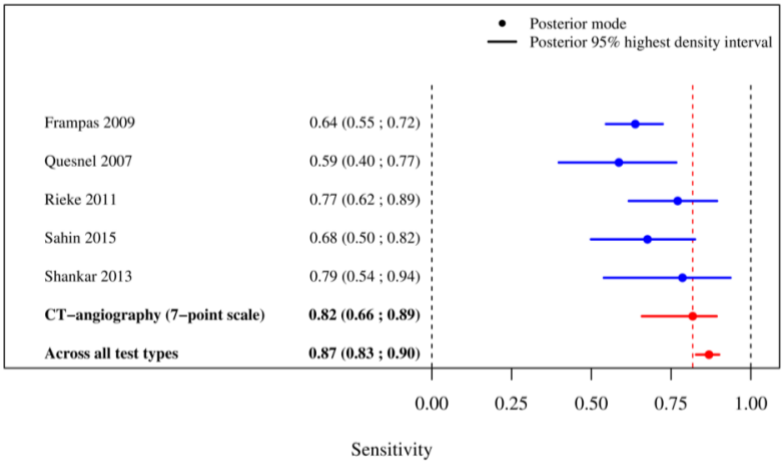
CA = cerebral anoxia, TBI = traumatic brain injury, ICH = intracranial hemorrhage, IS = ischemic stroke

CNA = cranial nerve areflexia, CP = central pain, PS = peripheral stimulation, AT = apnea test

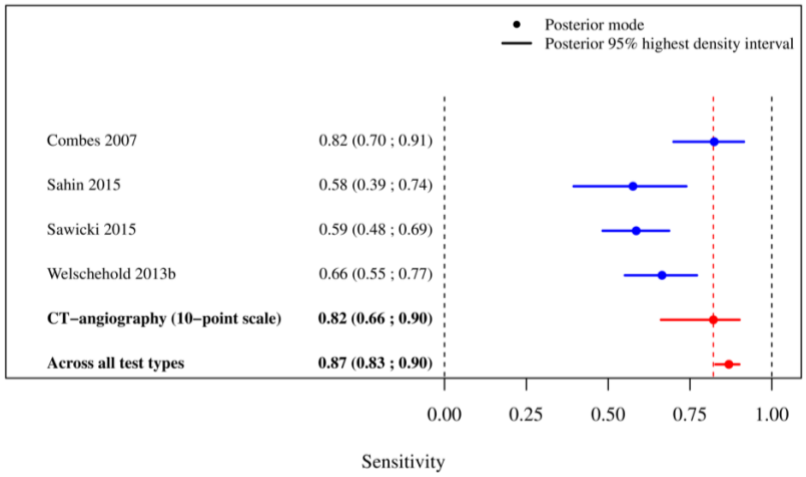
eFig. 1 Partially-pooled sensitivities by study for CTA (4 points) in the population of patients with death by neurologic criteria



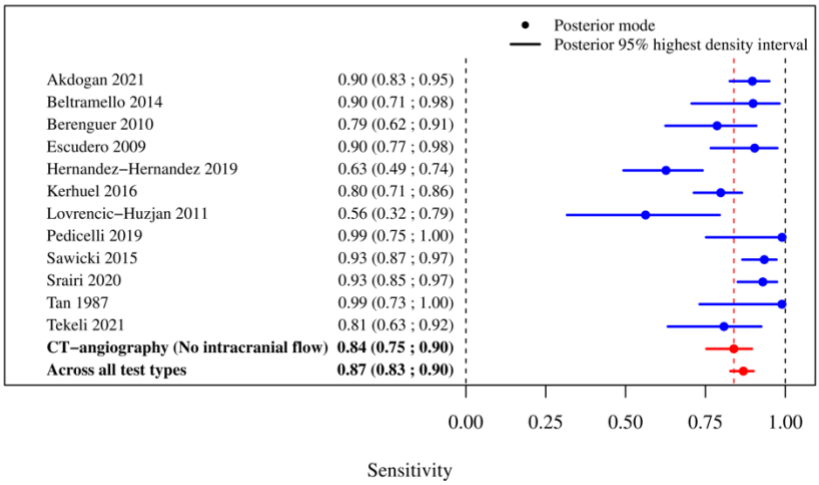
eFig. 2 Partially-pooled sensitivities by study for CTA (7 points) in the population of patients with death by neurologic criteria



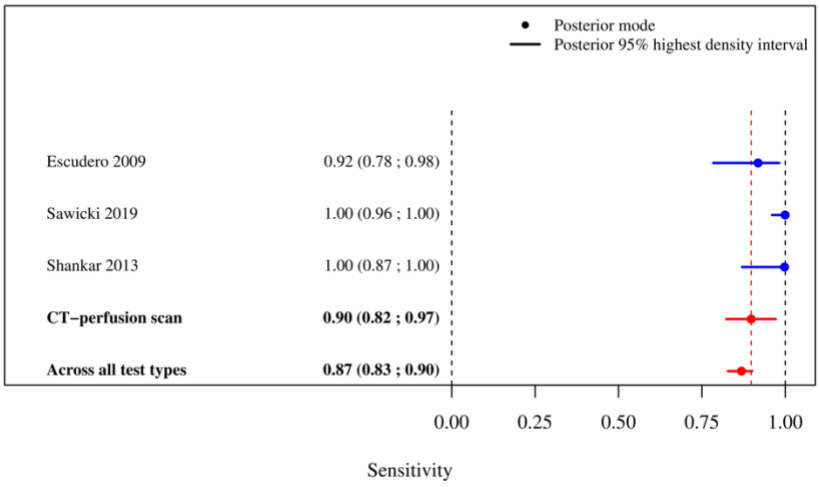
eFig. 3 Partially-pooled sensitivities by study for CTA (10 points) in the population of patients with death by neurologic criteria



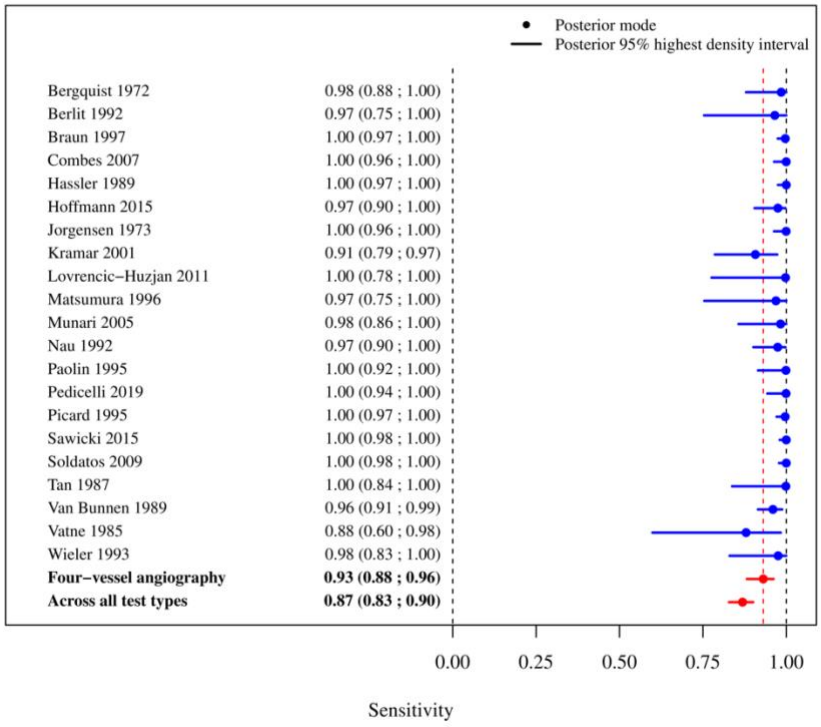
eFig. 4 Partially-pooled sensitivities by study for CTA (no intracranial flow) in the population of patients with death by neurologic criteria



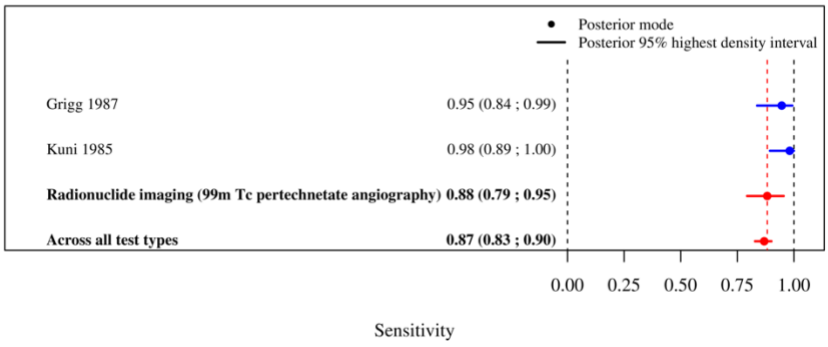
eFig. 5 Partially-pooled sensitivities by study for CT perfusion scan in the population of patients with death by neurologic criteria



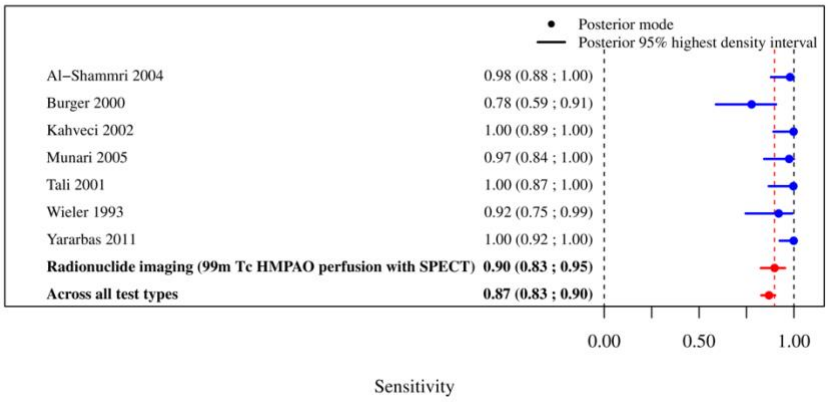
eFig. 6 Partially-pooled sensitivities by study for 4-vessel angiography in the population of patients with death by neurologic criteria



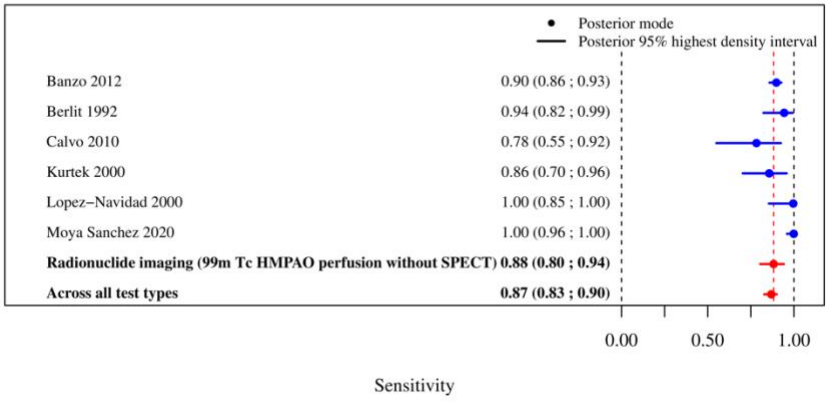
eFig. 7 Partially-pooled sensitivities by study for radionuclide imaging (99m Tc-pertechnetate angiography) in the population of patients with death by neurologic criteria



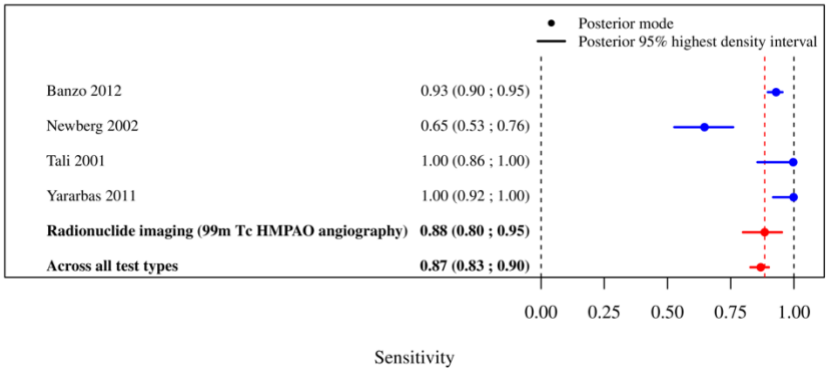
eFig. 8 Partially-pooled sensitivities by study for radionuclide imaging (99m Tc-HMPAO perfusion with SPECT) in the population of patients with death by neurologic criteria



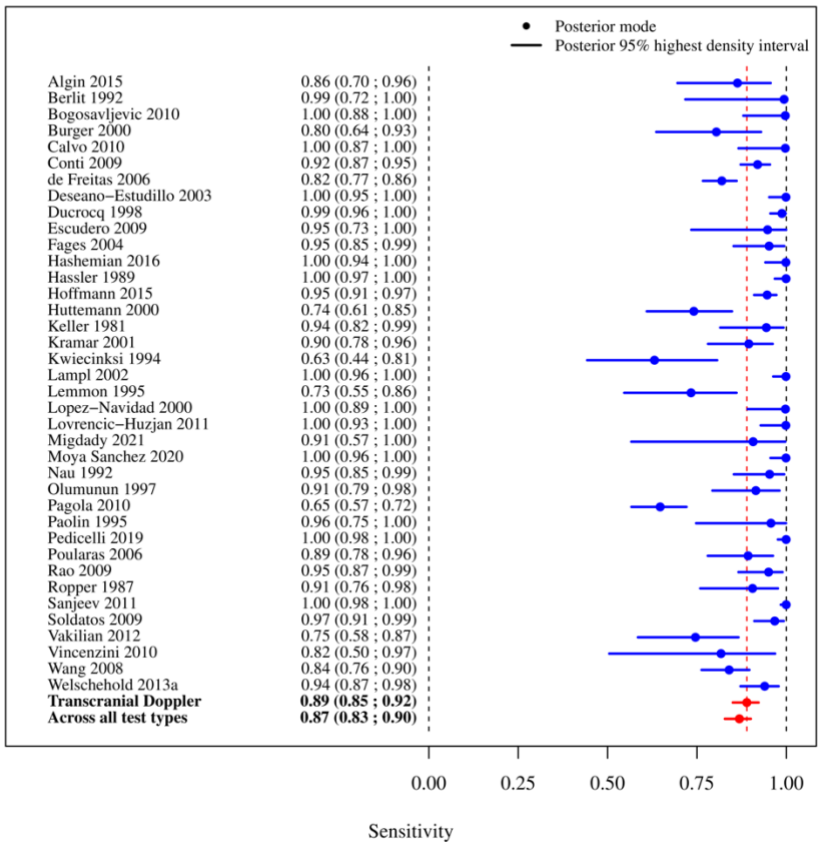
eFig. 9 Partially-pooled sensitivities by study for radionuclide imaging (99m Tc-HMPAO perfusion without SPECT) in the population of patients with death by neurologic criteria



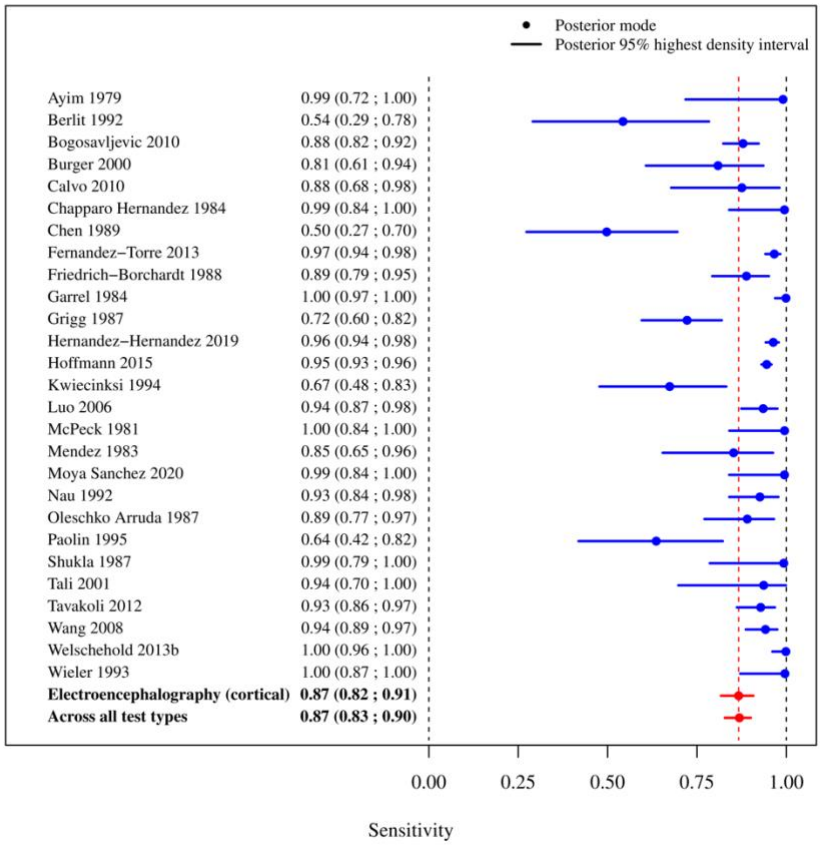
eFig. 10 Partially-pooled sensitivities by study for radionuclide imaging (99m Tc-HMPAO angiography) in the population of patients with death by neurologic criteria



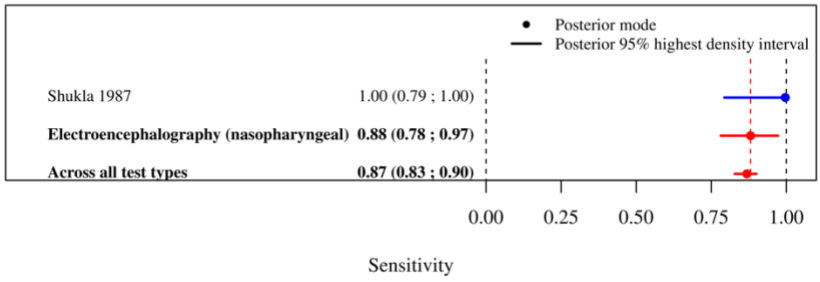
eFig. 11 Partially-pooled sensitivities by study for transcranial Doppler in the population of patients with death by neurologic criteria



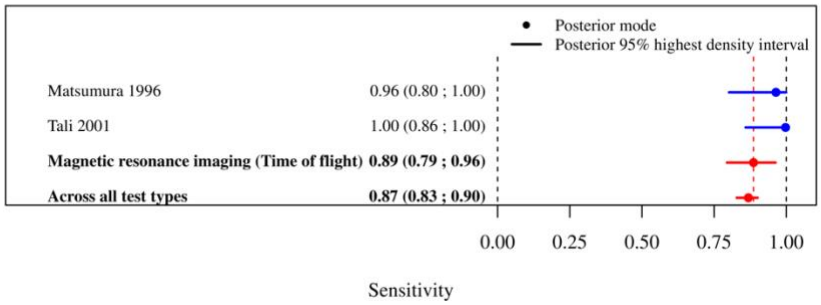
eFig. 12 Partially-pooled sensitivities by study for electroencephalography (cortical) in the population of patients with death by neurologic criteria



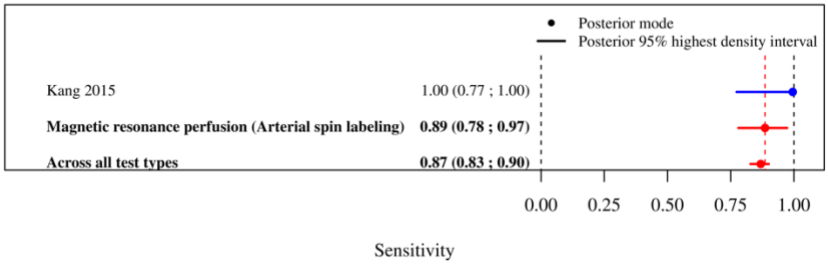
eFig. 13 Partially-pooled sensitivities by study for electroencephalography (nasopharyngeal) in the population of patients with death by neurologic criteria



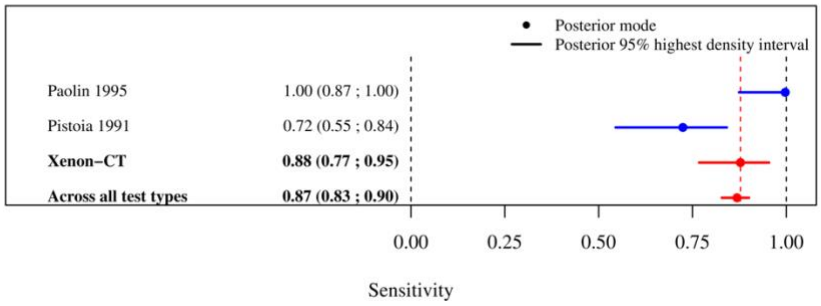
eFig. 14 Partially-pooled sensitivities by study for magnetic resonance imaging in the population of patients with death by neurologic criteria



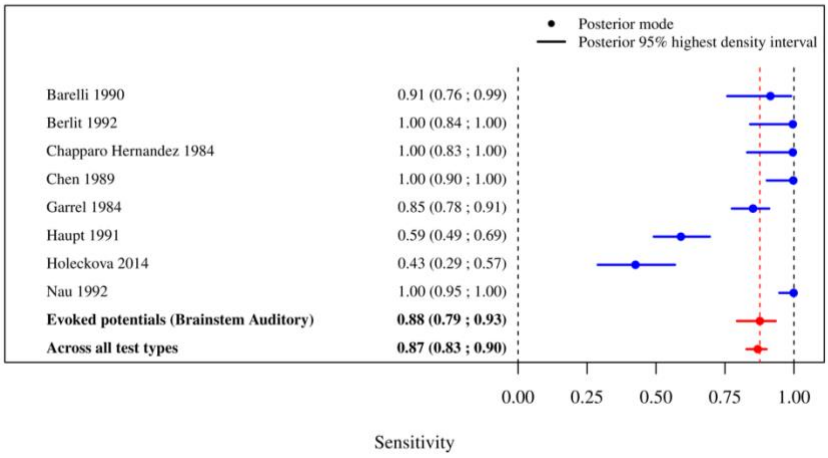
eFig. 15 Partially-pooled sensitivities by study for magnetic resonance perfusion (arterial spin labeling) in the population of patients with death by neurologic criteria



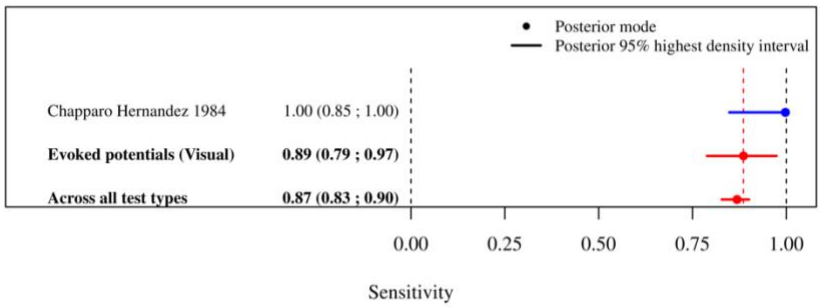
eFig. 16 Partially-pooled sensitivities by study for Xenon CT in the population of patients with death by neurologic criteria



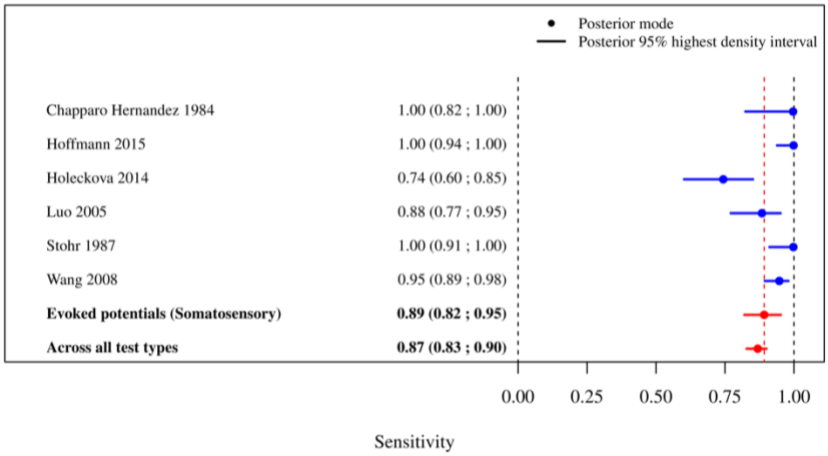
eFig. 17 Partially-pooled sensitivities by study for evoked potentials (brainstem auditory) in the population of patients with death by neurologic criteria



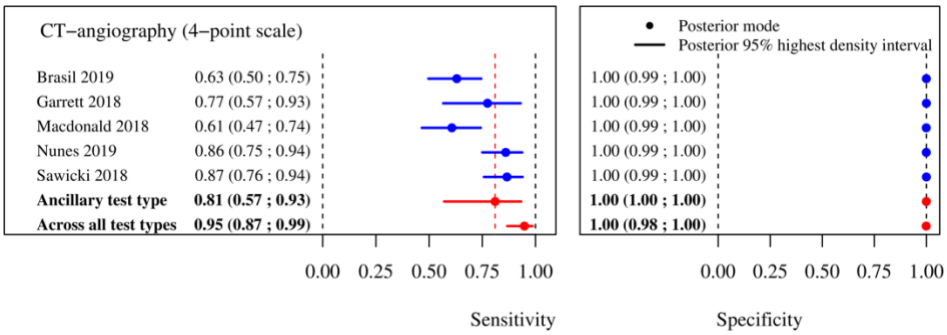
eFig. 18 Partially-pooled sensitivities by study for evoked potentials (visual) in the population of patients with death by neurologic criteria



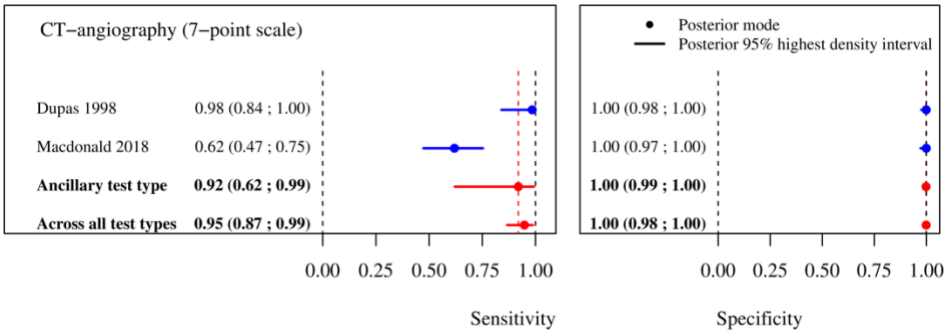
eFig. 19 Partially-pooled sensitivities by study for evoked potentials (somatosensory) in the population of patients with death by neurologic criteria



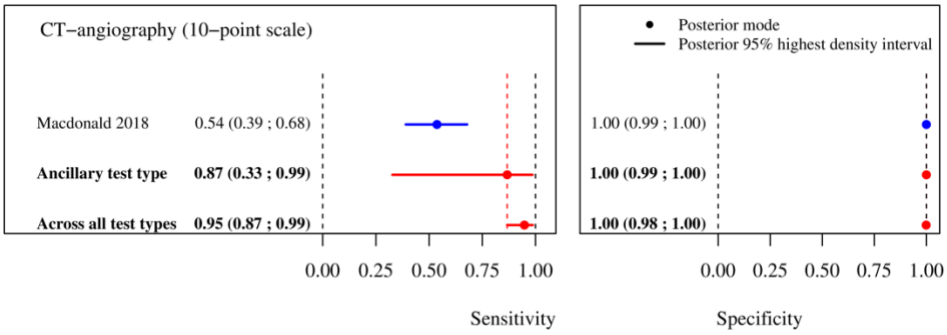
eFig. 20 Partially-pooled sensitivities and specificities by study for CTA (4 point) in the population of patients clinically suspected of death by neurologic criteria



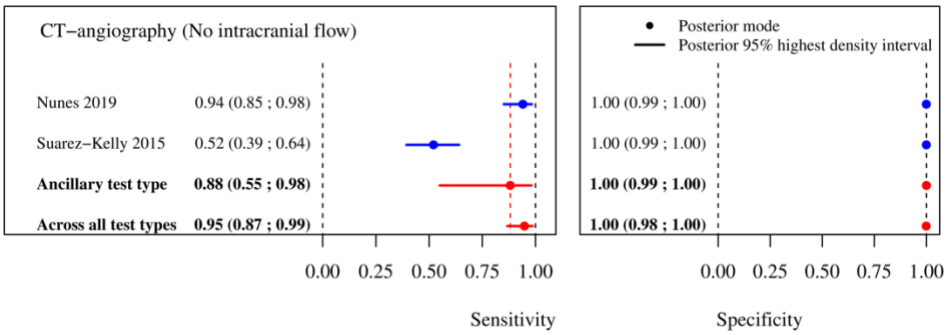
eFig. 21 Partially-pooled sensitivities and specificities by study for CTA (7 point) in the population of patients clinically suspected of death by neurologic criteria



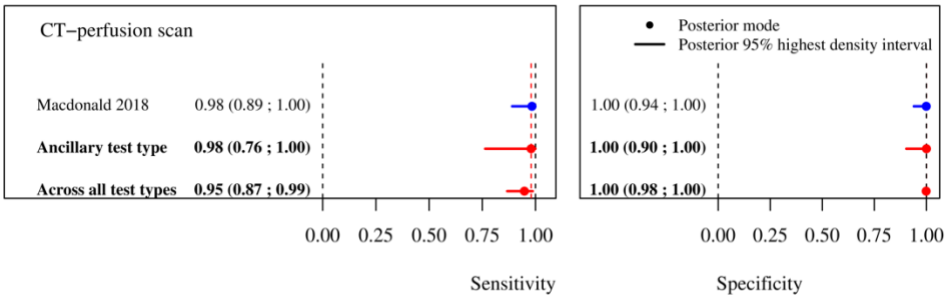
eFig. 22 Partially-pooled sensitivities and specificities by study for CTA (10 point) in the population of patients clinically suspected of death by neurologic criteria



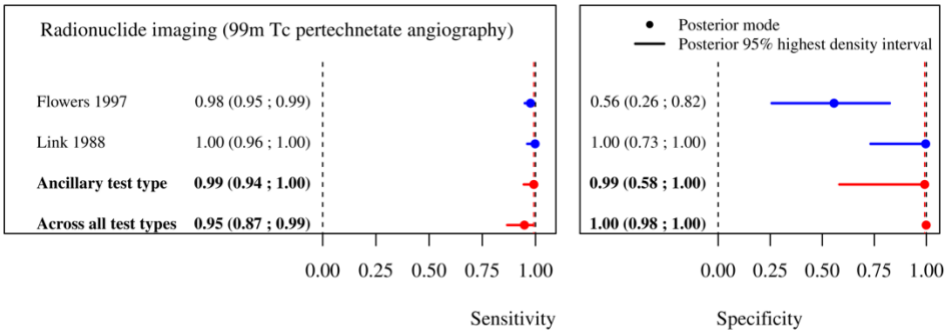
eFig. 23 Partially-pooled sensitivities and specificities by study for CTA (no intracranial flow) in the population of patients clinically suspected of death by neurologic criteria



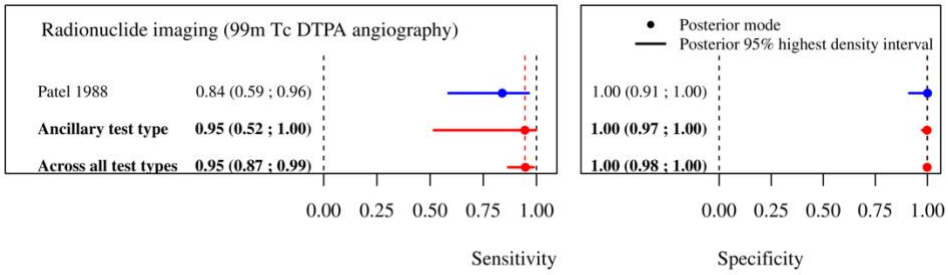
eFig. 24 Partially-pooled sensitivities and specificities by study for CT perfusion scan in the population of patients clinically suspected of death by neurologic criteria



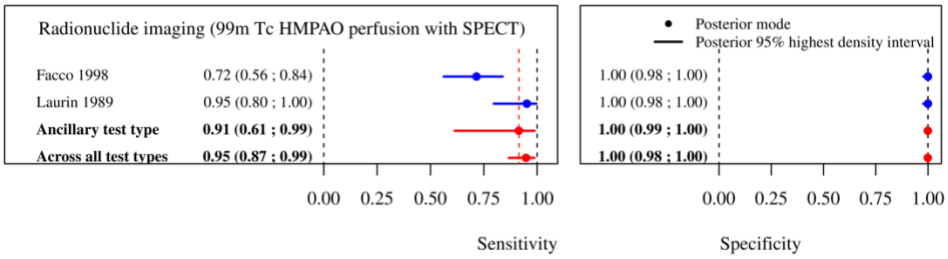
eFig. 25 Partially-pooled sensitivities and specificities by study for radionuclide imaging (99m Tc-pertechnetate angiography) in the population of patients clinically suspected of death by neurologic criteria



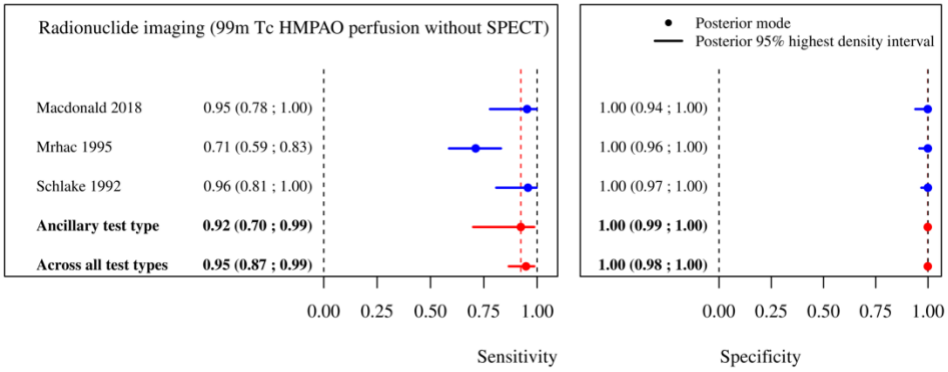
eFig. 26 Partially-pooled sensitivities and specificities by study for radionuclide imaging (99m Tc-DTPA angiography) in the population of patients clinically suspected of death by neurologic criteria



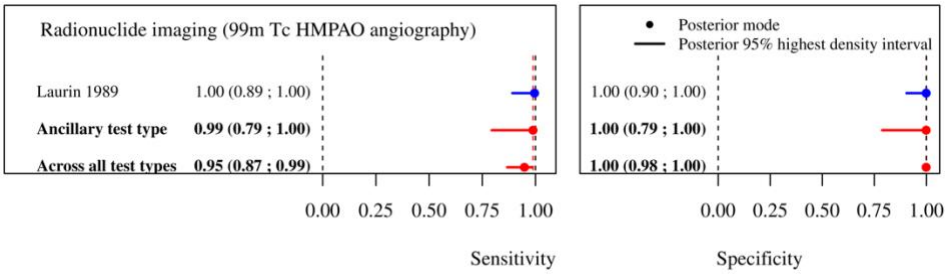
eFig. 27 Partially-pooled sensitivities and specificities by study for radionuclide imaging (99m Tc-HMPAO perfusion with SPECT) in the population of patients clinically suspected of death by neurologic criteria



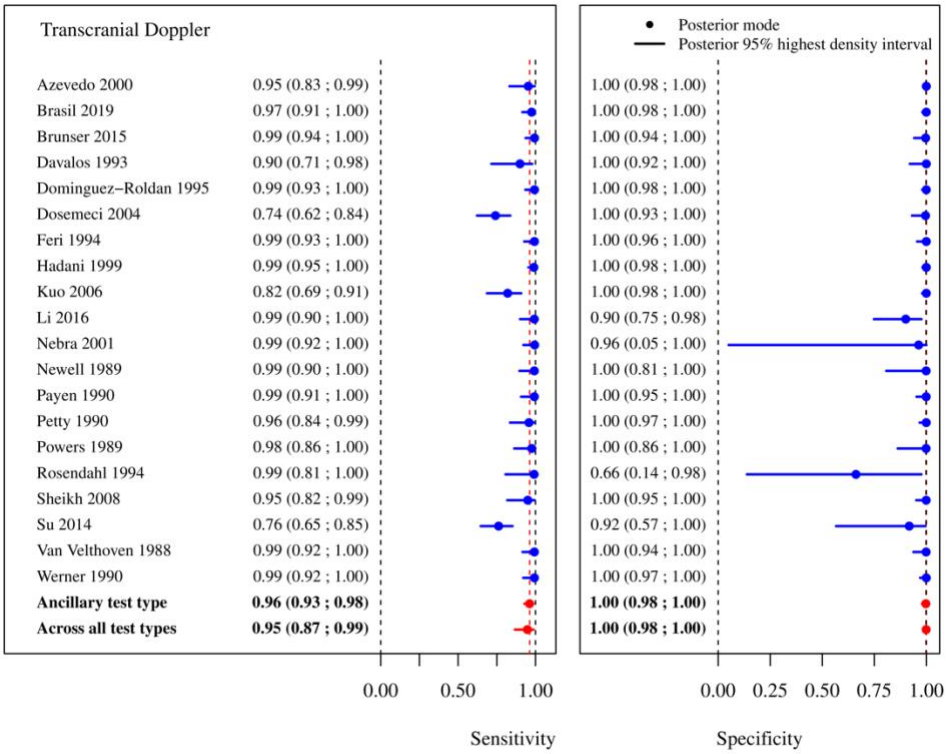
eFig. 28 Partially-pooled sensitivities and specificities by study for radionuclide imaging (99m Tc-HMPAO perfusion without SPECT) in the population of patients clinically suspected of death by neurologic criteria



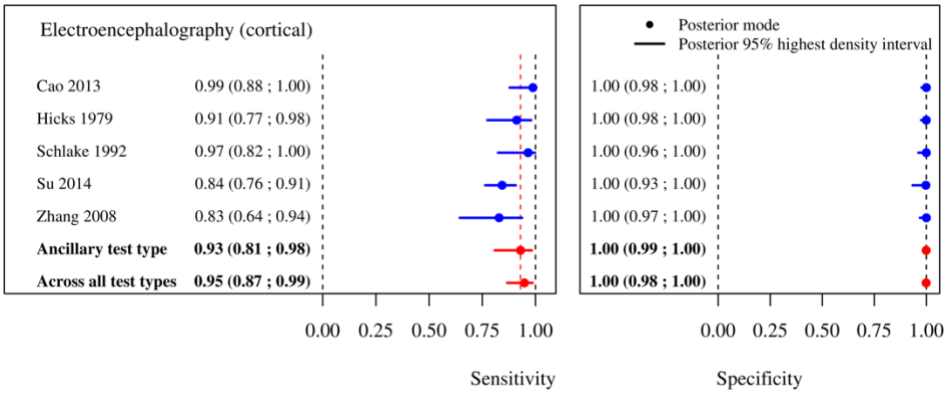
eFig. 29 Partially-pooled sensitivities and specificities by study for radionuclide imaging (99m Tc-HMPAO angiography) in the population of patients clinically suspected of death by neurologic criteria



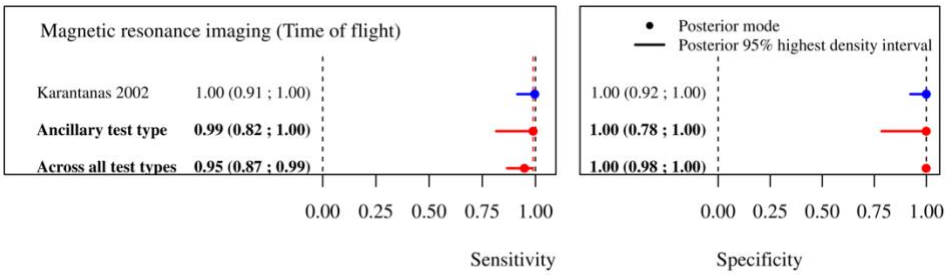
eFig. 30 Partially-pooled sensitivities and specificities by study for transcranial Doppler in the population of patients clinically suspected of death by neurologic criteria



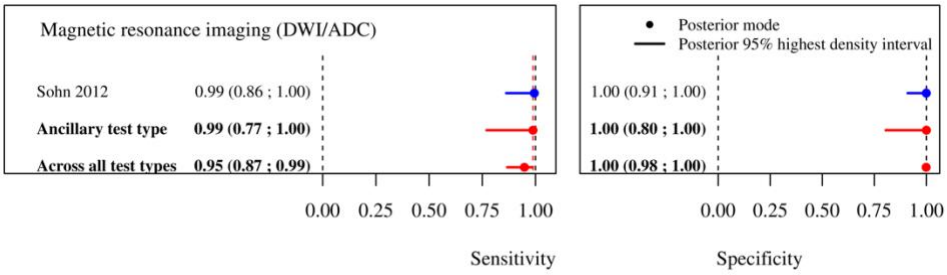
eFig. 31 Partially-pooled sensitivities and specificities by study for electroencephalography (cortical) in the population of patients clinically suspected of death by neurologic criteria



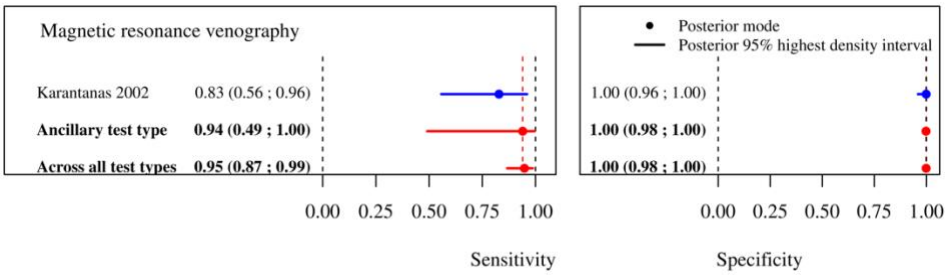
eFig. 32 Partially-pooled sensitivities and specificities by study for magnetic resonance imaging (time of flight) in the population of patients clinically suspected of death by neurologic criteria



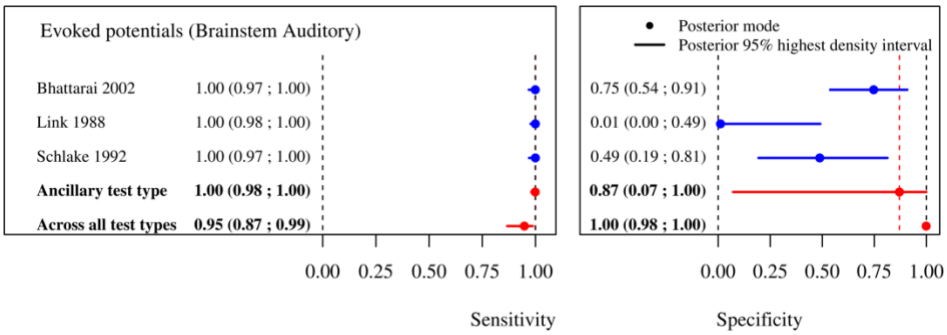
eFig. 33 Partially-pooled sensitivities and specificities by study for magnetic resonance imaging (DWI/ADC) in the population of patients clinically suspected of death by neurologic criteria



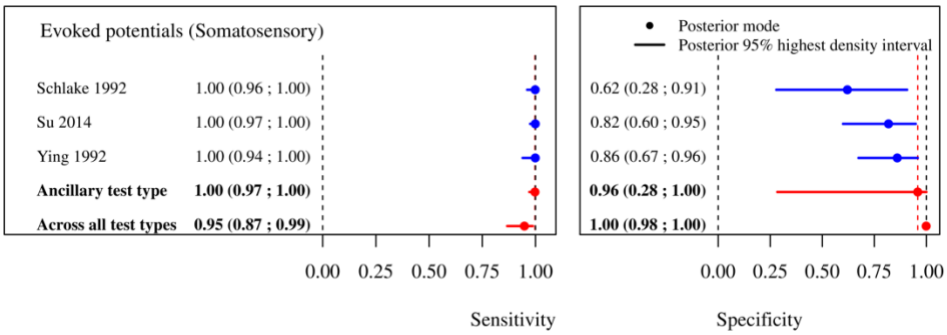
eFig. 34 Partially-pooled sensitivities and specificities by study for magnetic resonance venography in the population of patients clinically suspected of death by neurologic criteria



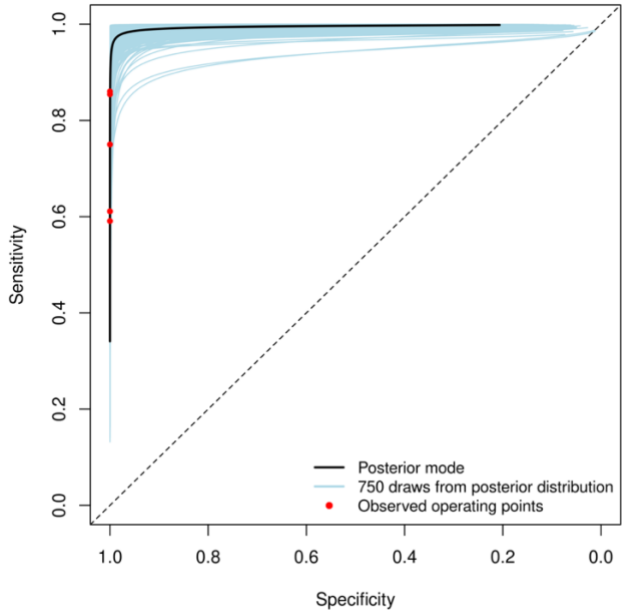
eFig. 35 Partially-pooled sensitivities and specificities by study for evoked potentials (brainstem auditory) in the population of patients clinically suspected of death by neurologic criteria



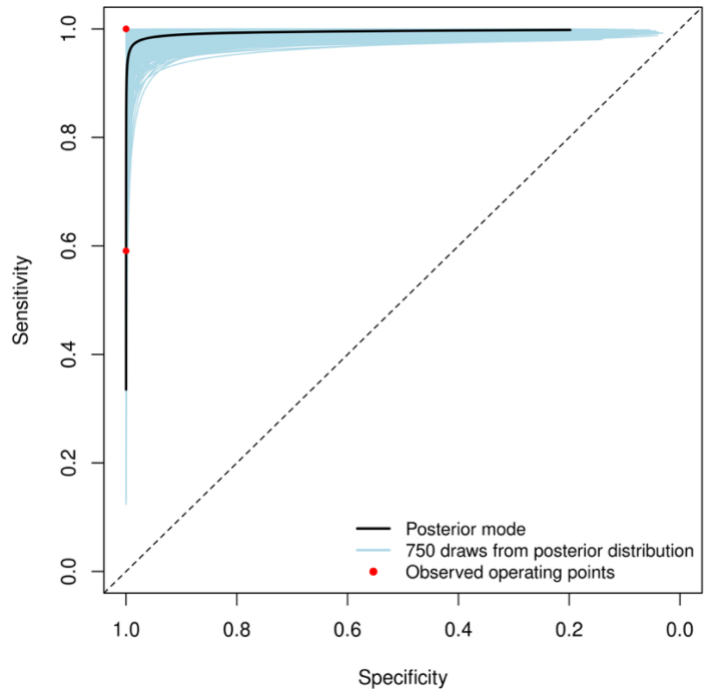
eFig. 36 Partially-pooled sensitivities and specificities by study for evoked potentials (somatosensory) in the population of patients clinically suspected of death by neurologic criteria



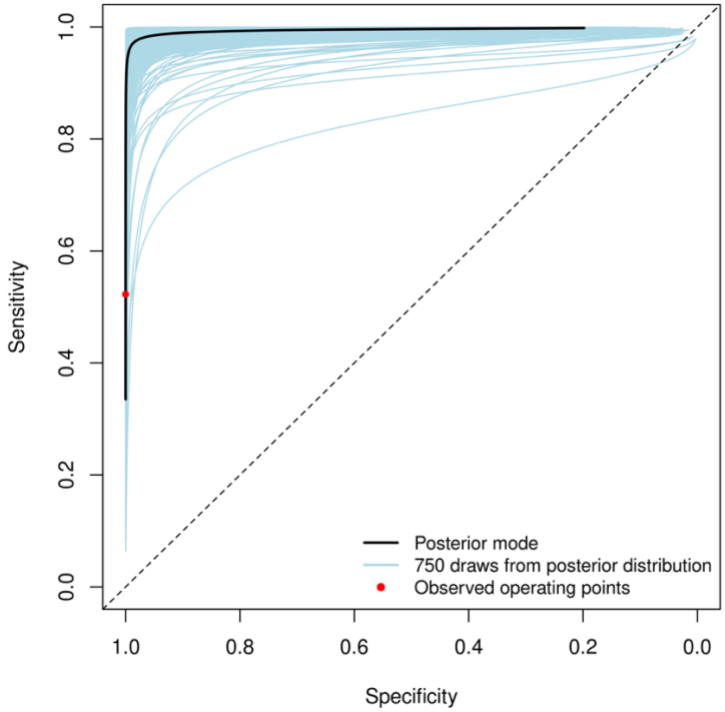
eFig. 37 Summary ROC curve estimates: CTA (4 point) in the population of patients clinically suspected of death by neurologic criteria



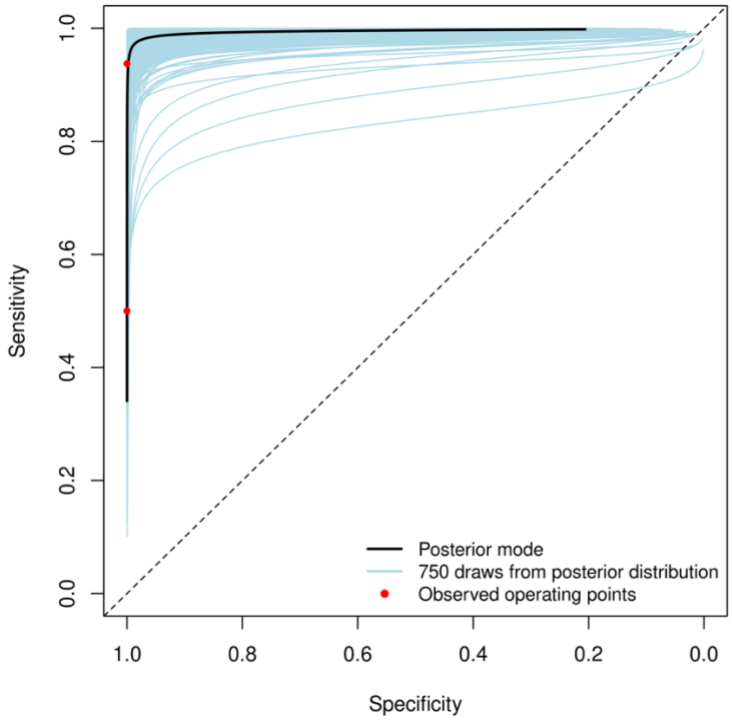
eFig. 38 Summary ROC curve estimates: CTA (7 point) in the population of patients clinically suspected of death by neurologic criteria



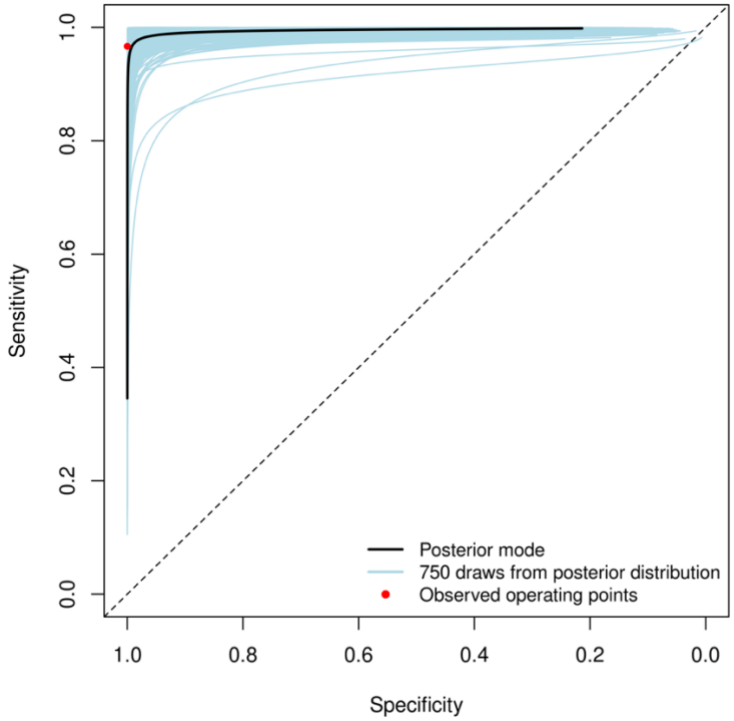
eFig. 39 Summary ROC curve estimates: CTA (10 point) in the population of patients clinically suspected of death by neurologic criteria



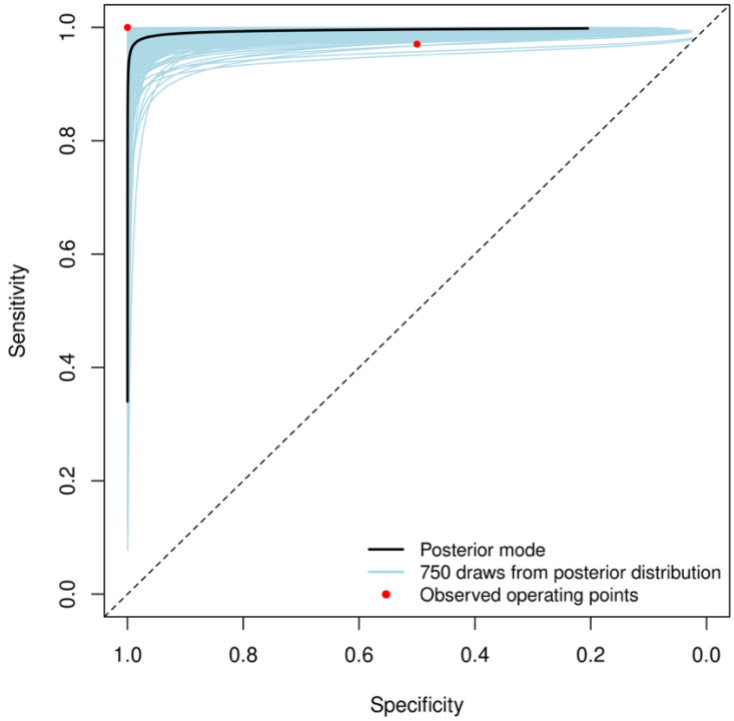
eFig. 40 Summary ROC curve estimates: CTA (no intracranial flow) in the population of patients clinically suspected of death by neurologic criteria



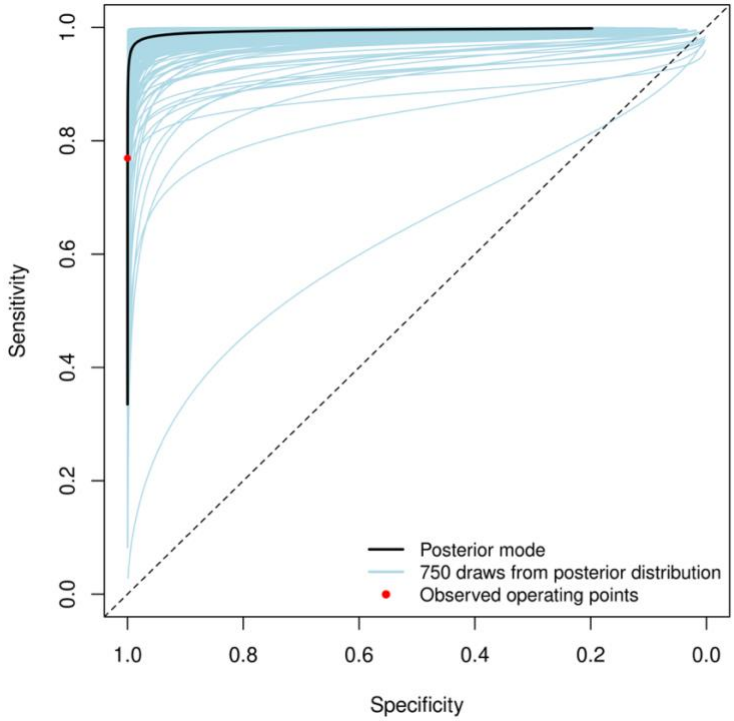
eFig. 41 Summary ROC curve estimates: CT perfusion scan in the population of patients clinically suspected of death by neurologic criteria



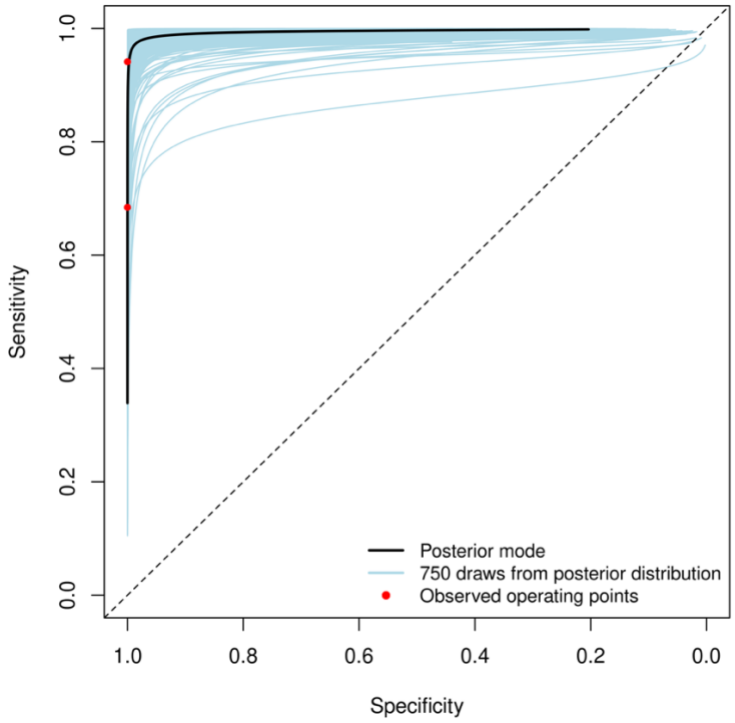
eFig. 42 Summary ROC curve estimates: Radionuclide imaging (99m Tc-pertechnetate angiography) in the population of patients clinically suspected of death by neurologic criteria



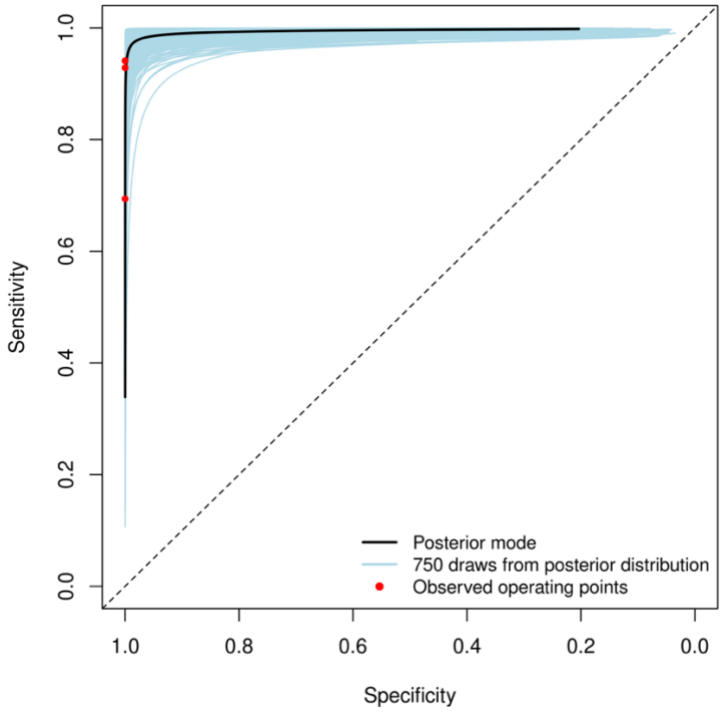
eFig. 43 Summary ROC curve estimates: Radionuclide imaging (99m Tc-DTPA angiography) in the population of patients clinically suspected of death by neurologic criteria



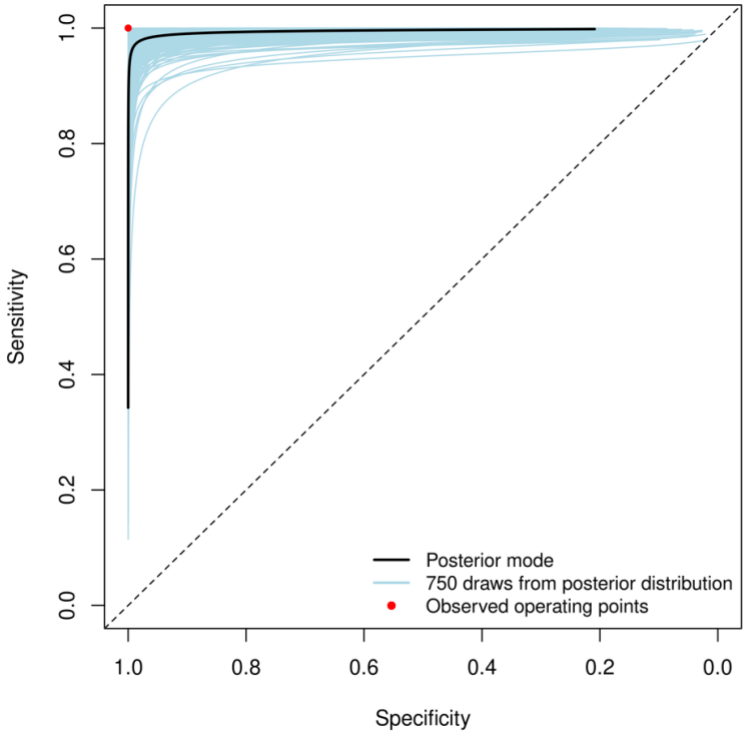
eFig. 44 Summary ROC curve estimates: Radionuclide imaging (99m Tc-HMPAO perfusion with SPECT) in the population of patients clinically suspected of death by neurologic criteria



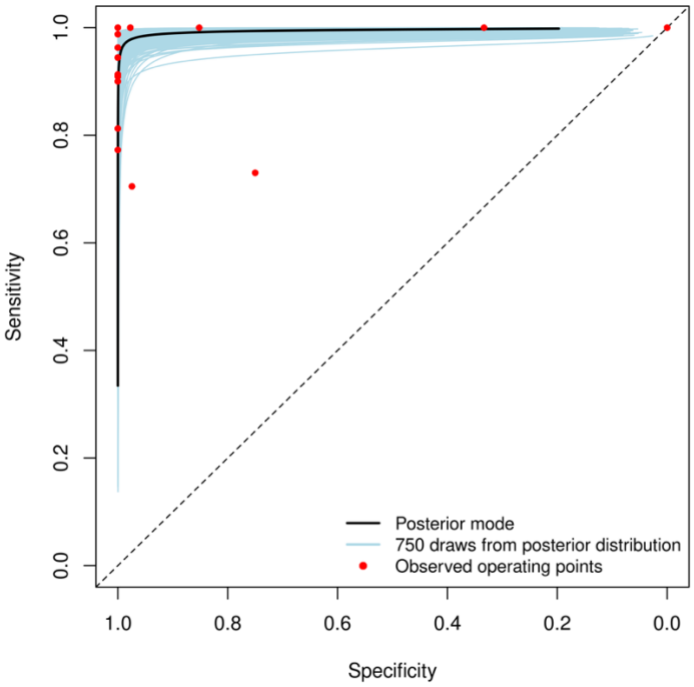
eFig. 45 Summary ROC curve estimates: Radionuclide imaging (99m Tc-HMPAO perfusion without SPECT) in the population of patients clinically suspected of death by neurologic criteria



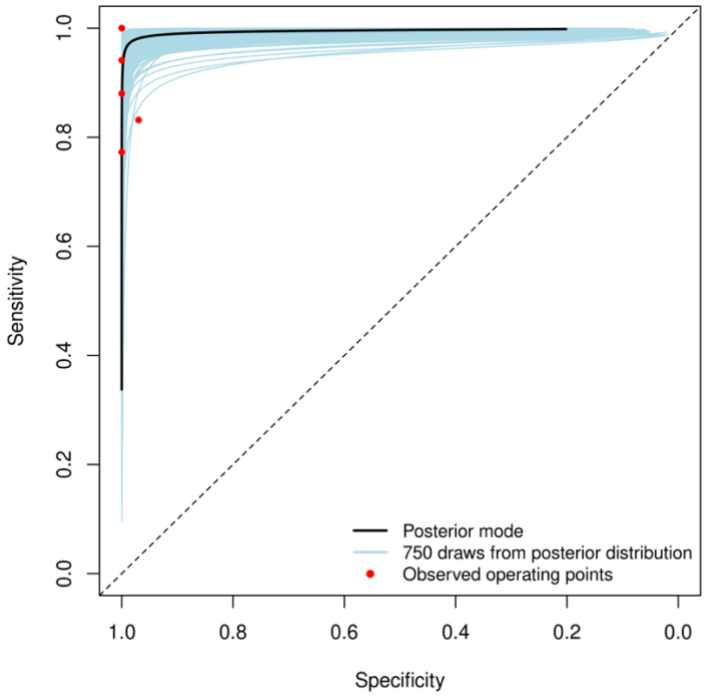
eFig. 46 Summary ROC curve estimates: Radionuclide imaging (99m Tc-HMPAO angiography) in the population of patients clinically suspected of death by neurologic criteria



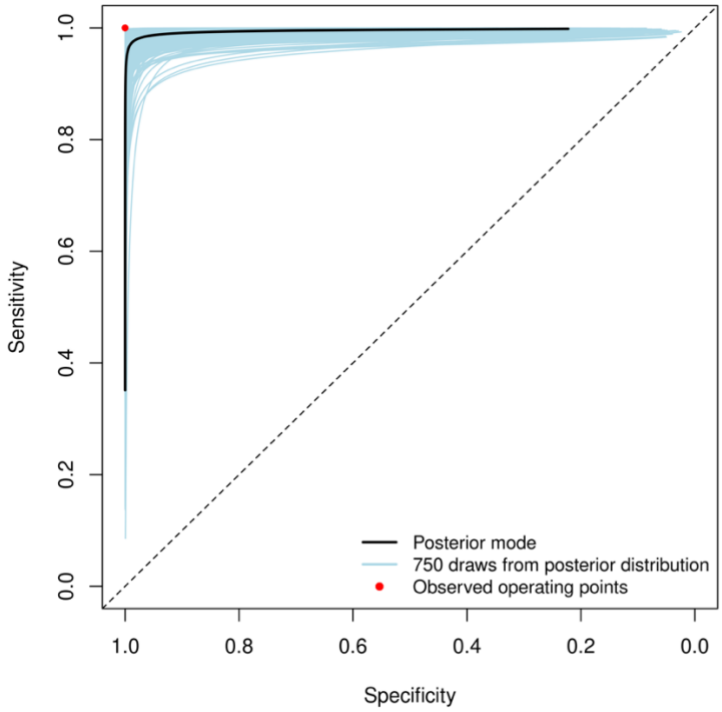
eFig. 47 Summary ROC curve estimates: Transcranial Doppler in the population of patients clinically suspected of death by neurologic criteria



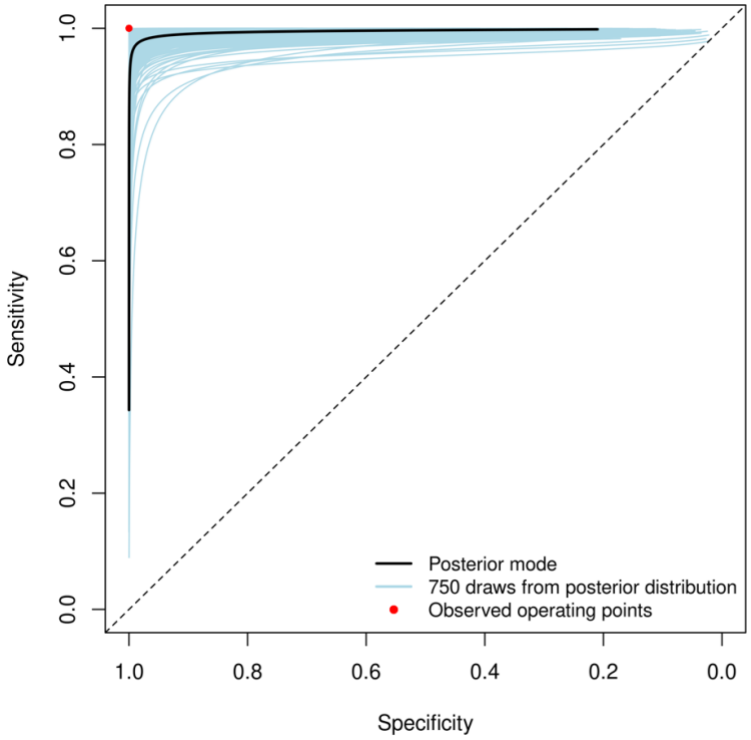
eFig. 48 Summary ROC curve estimates: Electroencephalography (cortical) in the population of patients clinically suspected of death by neurologic criteria



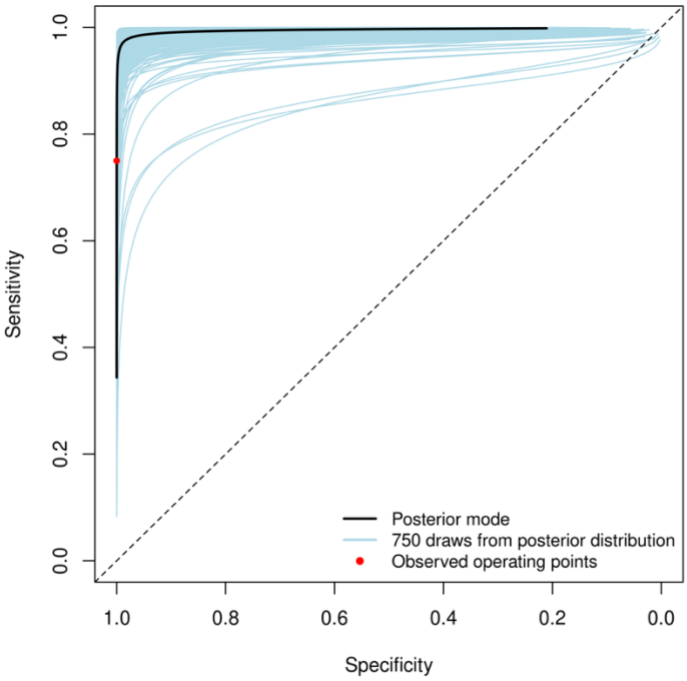
eFig. 49 Summary ROC curve estimates: Magnetic resonance imaging (Time of flight) in the population of patients clinically suspected of death by neurologic criteria



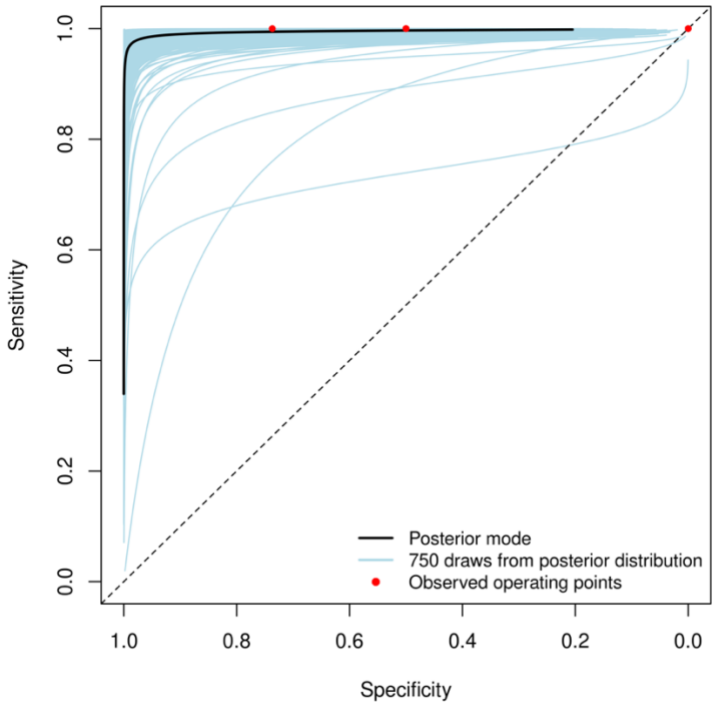
eFig. 50 Summary ROC curve estimates: Magnetic resonance imaging (DWI/ADC) in the population of patients clinically suspected of death by neurologic criteria



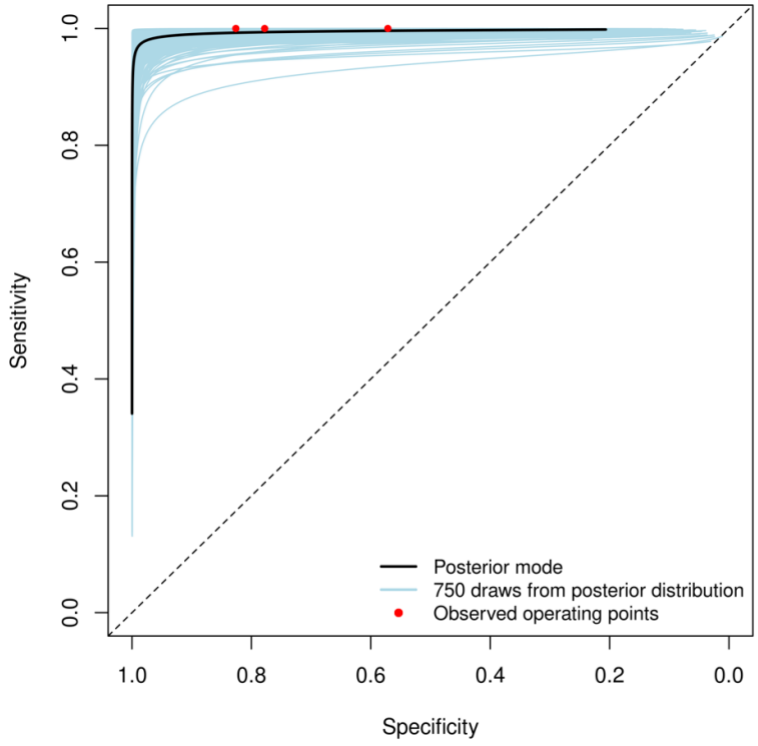
eFig. 51 Summary ROC curve estimates: Magnetic resonance venography in the population of patients clinically suspected of death by neurologic criteria



eFig. 52 Summary ROC curve estimates: Evoked potentials (Brainstem Auditory) in the population of patients clinically suspected of death by neurologic criteria

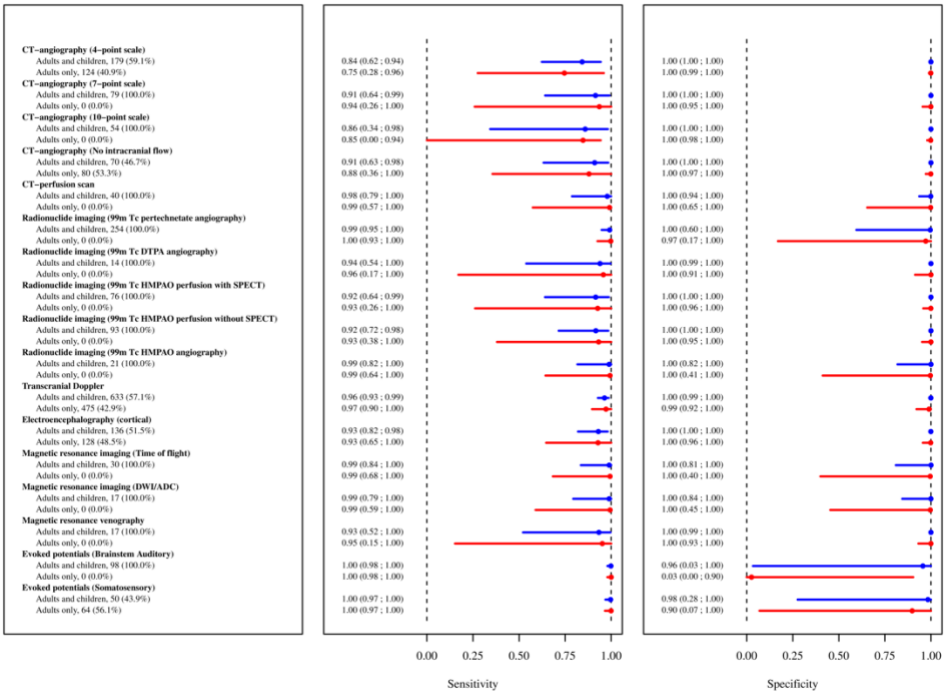


eFig. 53 Summary ROC curve estimates: Evoked potentials (Somatosensory) in the population of patients clinically suspected of death by neurologic criteria

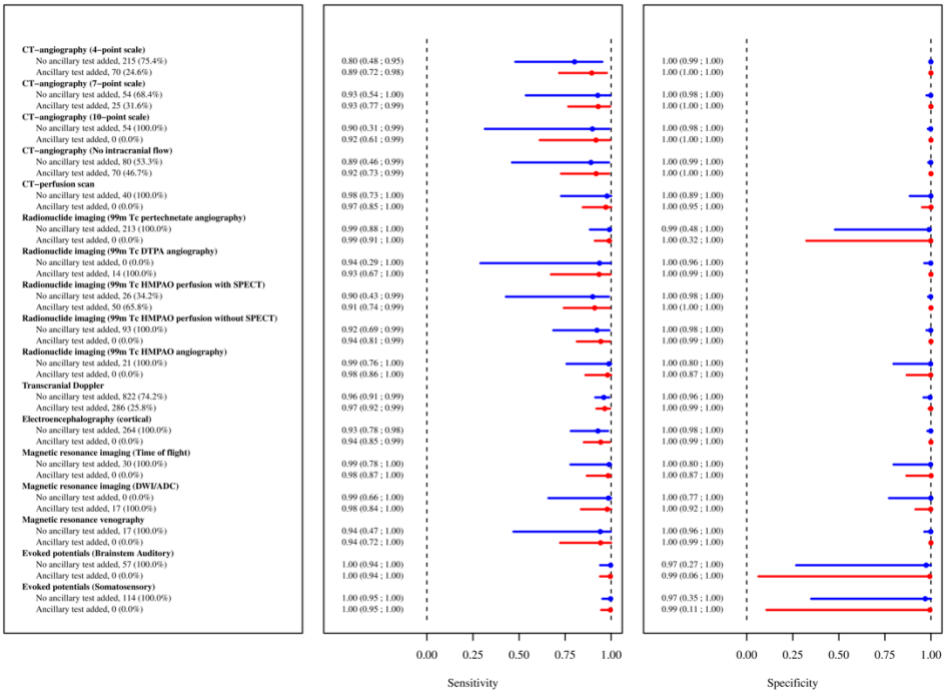


eFig. 54 Subgroup analyses of partially-pooled sensitivities and specificities in the population of patients clinically suspected of death by neurologic criteria by (a) demographic group, (b) inclusion of an ancillary test in the clinical diagnosis reference standard, and (c) presence of clinical examination confounders

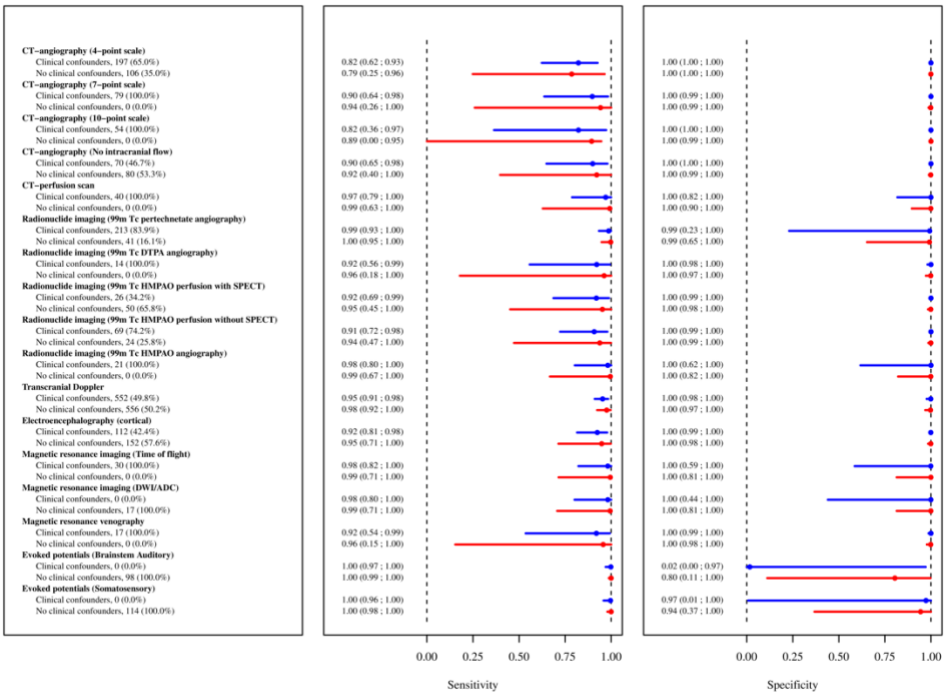
(A)



(B)



(C)



ADC = apparent diffusion coefficient; DTPA = diethylenetriamine pentaacetate; DWI = diffused weighted imaging; HMPAO = hexamethylpropyleneamine oxime; SPECT = single-photon emission computed tomography

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